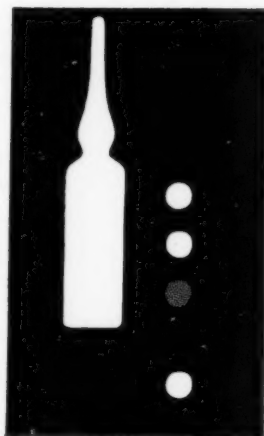


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Manufacturing Chemist

Editor: W. G. Norris

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THE FACTORY MANAGER LIKES IT

THE GLASS MANUFACTURER LIKES IT



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TOPICS AND COMMENTS

New fatty acid techniques

GLYCERIDE oils and fats continue to be the major source of fatty acids, and fat splitting—generally hydrolysis of glycerides to give glycerol and fatty acids—is still an important process employed in this reaction. Precise knowledge about physico-chemical properties of fatty acids and the mechanism of the fat-splitting reaction have resulted in a vast improvement in these processes. For example, the batch autoclave catalytic method of fat-splitting has been developed into a continuous high-pressure method and the expensive operation of separating the fatty acids by hydraulic pressing has been replaced by low-temperature solvent crystallisation as represented by the *Emersol* process. At a recent symposium on developments in the manufacture and utilisation of fatty acids held at the Department of Chemical Technology, University of Bombay, S. N. Modak surveyed recent advances in fat-splitting technology. The most important processes used are Twitchell, low pressure autoclave and high pressure autoclave, both batch and continuous.

The Twitchell process which is still very widely used is in constant need of active catalysts. Originally Twitchell catalysts were prepared by sulphonating a mixture of oleic acid and aromatic hydrocarbons. These were gradually replaced by the sulphonated products obtained as by-products in petroleum refining. The catalysts of the alkyl-aryl type are the most efficient and are reputed to give a 90% split in about 8 hr. The splitting process became more efficient through the use of autoclaves by means of which higher reaction temperatures are possible. The present trend in fat-splitting is to use higher temperatures of the order of 220°C. to 260°C. corresponding to steam pressures of 350 to 700 p.s.i. This has been made possible because of newly-developed molybdenum-containing stainless steels which can withstand the corrosive action of fatty acids at high temperatures. At such temperatures, without the use of catalyst 90% split can be obtained in 2½ hr. as against 10 hr. in low-pressure autoclave and 30 to 40 hr. in the Twitchell process.

The crude fatty acids obtained after splitting contain a variety of fatty acids as well as unsplit fat, unsaponified matter, colouring matter and impurities present in the original oil. The following processes are used to refine the crude fatty acids:

- (i) simple distillation
- (ii) fractional distillation
- (iii) separation of unsaturated and saturated fatty acids.

Distillation is usually carried out under a vacuum of 2 to 10 mm. Hg. In view of the fact that fatty acids are heat sensitive it is most important to avoid

prolonged heating in excess of 15 min. The oldest and still most widely used process of separating stearic and oleic acid, for instance, is by pressing a suitable blend of tallow fatty acids. For example, when the blend contains stearic and palmitic in the ratio 55:45, the cake to be pressed becomes quite porous and oleic acid can be squeezed out at lower pressures. This process, however, is fast being superseded by the *Emersol* process. In this a solvent, aqueous methanol, is used to effect the separation of the unsaturated from the saturated fatty acids; the former dissolves in the solvent while the latter crystallises out and is separated by filtration.

Russian inventions

THE spate of Russian technical literature at present translated into English seems to be increasing rapidly. This, of course, is one more proof that the English-speaking world is slowly grasping the unmistakable fact that the Soviet Union is in the forefront of technical and scientific developments, not only in sputnik production but in more humble matters. Naturally no country can afford to carry out industrial research and reap its fruits if it does not recognise the validity of patent rights. It is therefore pleasing to note that the application and granting of patents is now beginning to be taken as seriously in the Soviet Union as it is in the West.

Pergamon Press have just published the first issue of a new monthly journal called *U.S.S.R. Patents and Inventions*, a translation from the Russian journal *Biulleten' Izobretenii*. Altogether 17 categories of manufacture have been selected covering chemistry, chemical engineering, mechanical and electrical engineering, agriculture, electronics, metallurgy, mining, measuring instruments, civil engineering, industrial gases, textile technology, building industry, fuels, food technology, public health, paper technology, precision engineering and aeronautics. Each category contains about 60-80 patent abstracts. It must be assumed in fact that this is only a random selection of typical specifications in these categories.

The category on chemistry and chemical engineering is very broad and covers all facets of the chemical industry. It would be impossible to review critically every patent mentioned in this section and we can only make general comments on some trends in the Russian chemical industry. Most of the specifications indicate that there is very little difference between the Western and the Soviet chemical industry. Fluidised bed catalysts, for instance, are being used in the oxidation of sulphurous anhydride. Terephthalic acid manufacture (the raw material for Terylene) warrants a special mention. An interesting specification describes corrosion-resisting linings

based on metallic oxides; in order to confer ductility on the lining, metal resinates have been added to its composition. A vertical evaporating apparatus is described which has a separator for vapour-liquid emulsion and a conduit for return of the separated liquid into the evaporator. A rectification plant is described for alcohol mixtures in which contact between vapour and liquid is set up by atomising the liquid using the vapour, whereupon the mixture which has been formed is subjected to separation.

The journal will appear monthly but it is very doubtful whether private subscribers could afford the very expensive annual subscription rate of £50. However, subscriptions to sections are also accepted and they cost £15. Nevertheless the journal will be of immense value to libraries and similar institutions. It is to be hoped that the time is not too distant when the Soviet Union will join the International Patent Convention and accept the privileges and obligations of this body.

Music in all things

In *Don Juan* Byron declaims:

There's music in the sighing of a reed;
There's music in the gushing of a rill;
There's music in all things, if men had ears:
The earth is but an echo of the spheres.

These lines must have inspired that audacious Harvard mathematician-turned-entertainer Mr. Tom Lehrer, for his latest song is about the periodic table, of all things. We scarcely believed our ears when we heard the record. The song is prefaced with a thoughtful comment that to most people chemical periodicity *per se* is far too dry and badly needs livening up. As a result 102 elements are declaimed, to suitable pianoforte accompaniment, at a tempo of *allegro molto vivace*. Mr. Lehrer's grouping is solely according to rhythmic merit—quite pleasing to our sense of jingle, though we doubt whether altogether acceptable to the International Union of Pure and Applied Chemistry. This homage to chemistry concludes with a most appropriate summary, and here we quote from memory:

These are all the elements known to Harvard,
There may be others but they haven't been discovered.

As a first step in bringing science to the masses this seems to us quite unsurpassed. We await further improvisations in the arena of the classroom. Then grubby young fifteen-year-olds will cease to bewail the difficulty of memorising the relationship between beryllium and francium but, on the contrary, will tap it out to the latest rock rhythm.

Changes at the top

WITHIN a matter of months changes have occurred or have been announced in the top management of three of Britain's biggest companies. I.C.I.'s new chairman, Mr. S. P. Chambers, has been in the saddle since March. Mr. George Cole has been

chairman of Unilever since April 26. And now Boots' chairman, Mr. John Percival Savage, announces that next March he will retire after seven years in office, during which time sales have risen by over 60%, profits 2½ times and some £15 million have been spent on capital development. This is a fine legacy to leave to his successor, who will be once more a member of the Boot family. Mr. Willoughby Rollo Norman is the son-in-law of the late Lord Trent, son of Jesse Boot who founded the company 72 years ago. He is an ex-Grenadier Guardsman and has been an underwriting member of Lloyds since 1933. He is just over 50 and clearly has a good period of years ahead to develop his great company.

There is an interesting and significant link between Mr. S. P. Chambers and the managing director-designate of Boots, Mr. Francis Arthur Cockfield. Mr. Cockfield, still in his early forties, succeeded Mr. Chambers as director of statistics and intelligence at the Inland Revenue in 1945. In 1951 he became a Commissioner of Inland Revenue and his formidable talents in the field of finance and taxation have been of great benefit to Boots, whom he joined in 1952, soon afterwards becoming finance director. The management of a company with a turnover now over £90 million requires all the financial expertise of a former Commissioner of Inland Revenue, not least in matters of taxation which are such a weighty burden on industry these days.

For his deputy managing director Mr. Cockfield will have Mr. Kenneth Dyball Williamson, a veteran of Boots. He is a barrister and has spent his 30 years at Boots in various buying departments.

Corrosion and Metal Finishing Exhibition

THE Organisers of the Corrosion Exhibition have for some time given consideration to a new name that would better express the purpose and content of this important and increasingly popular show. They have taken into account the fact that a great many exhibitors sell products that both protect and finish metals. In many cases corrosion-protection and metal finishing are inseparable and implicit. After a great deal of discussion and consultation they have decided to make explicit that which is already implicit and have chosen the amplified name of: The Corrosion and Metal Finishing Exhibition. Thus the Corrosion Exhibition, like all vigorously growing enterprises, enters a new phase of its existence. Everything that made a success of the Corrosion Exhibition is retained. Everything is being done to widen its appeal and draw the right kind of visitors to Olympia from November 29 to December 2.

An encouraging and significant feature is the growing official support for the Exhibition. The Corrosion Group of the S.C.I. have accepted the Organiser's invitation to hold a meeting at Olympia

during the Exhibition. The subject will probably be: "The Influence of Water Movement on Corrosion." Plans are being made for the participation of other professional and technical bodies and Government departments concerned with corrosion and metal finishing. Already the D.S.I.R. and the Atomic Energy Authority are exhibiting.

Publicity for the exhibition is well under way. It will embrace the total resources of the Leonard Hill technical publications, and the technical and national press, direct mail and editorial features.

Already the Exhibition is heavily booked and with its widened appeal consideration is being given to providing further space in the Empire Hall, Olympia. Intending exhibitors are urged to write or phone now to book their stands. Contact: The Director, The Corrosion and Metal Finishing Exhibition, 9 Eden Street, London, N.W.1, Euston 5911.

Plant export problems

A CERTAIN unease felt by the chemical plant industry is reflected in the annual report of the British Chemical Plant Manufacturers Association for 1959. Imports of chemical and gas machinery plant in 1959 came to 904 tons at a value of £0.84 million, considerably less than those for 1958, which totalled 1,296 tons at a value of £1.28 million. In contrast, exports rose during the same period:

	Tons		£ million	
	1958	1959	1958	1959
Gas and chemical machinery ..	12,219	7,424	5.26	5.45
Plastics and rubber working machinery ..	7,832	14,714	4.68	9.76
Total chemical and allied plant ..	28,527	30,830	14.70	20.17

This increase, however, is almost entirely due to the very steep rise in exports of plastics and rubber working machinery due to the Russian tyre plant which a British consortium is erecting.

The economic division of Europe is beginning to cause anxiety to chemical plant constructors. The report mentioned particularly that during the preliminary stages of the discussions leading to the European Free Trade Association (the Outer Seven) the government sought the views of the BCPMA, which indicated that the chemical plant industry was prepared to acquiesce in these negotiations on the understanding that the formation of some acceptable trading association with the European Economic Community would thereby be facilitated. This qualification was important to many members who considered that EFTA offered no immediate direct benefit on its own. With the exception of Austria and Norway, for instance, other countries in the Outer Seven have much lower tariffs than the United Kingdom and they would therefore benefit much more from a percentage reduction in tariffs. The volume of trade in chemical plant between the U.K. and other members of the Outer Seven is not high, exports to these countries in 1958 totalled £0.45

million or 3% of all exports. During the same period 8% was exported to the six countries of the European Economic Community.

These figures speak for themselves and it seems that at present the only hope is to develop the Outer Seven export market which has a larger potential than appears from the figures quoted above. Nevertheless one does hope, for the benefit of industry at large, that the government has not and does not intend to burn all its bridges with the E.E.C.

Unification in chemical engineering

In science and technology the trend is to unify rather than divide, because only unification can demonstrate certain similarities between various systems. A good example of increasing comprehension as a result of unification can be seen in the field of mass-transfer operations. Hitherto unit operations in chemical engineering have been treated as self-contained entities; distillation, evaporation, absorption, for example, all grew up in different circumstances and previously the analysis of these reactions was often quite pragmatic. Lately a tendency has grown to group those operations involving similar phases into one category.

Taking the solid-fluid phase of mass transfer, operations in this category include adsorption, drying and leaching. Whereas adsorption involves contact of solids with either liquids or gases with mass transfer in the direction fluid to solid, drying involves gas-solid and leaching liquid-solid contact with mass transfer in each case in the direction solid to fluid. Thus, theoretically at least, similar plant used for gas-solid or liquid-solid contact in adsorption should be correspondingly useful for drying and leaching. In practice, however, different types of equipment are to be found in all three operations—this undoubtedly is due to the fact that each has a different historical background. Drying, for example, has been used for centuries in the manufacture of pottery and ceramics. Similarly leaching, although not as ancient an art as drying, has been used extensively in extraction of fats from groundnuts and in many other processes in food manufacture. In contrast to this, adsorption is a relative newcomer and only during the past 30 years has the importance of solvent recovery based on adsorption been fully understood, with the result that unification of these three operations is becoming increasingly fruitful.

The industrial importance of solvent recovery cannot be over-stressed. We hear much nowadays about solvents recovered being equivalent to money saved, but this has certainly not been fully appreciated by those who could best benefit by it. The total consumption of solvents by British industry in 1959 was approximately 700 million gal. One of the largest applications of solvent recovery is in the production of regenerated cellulose, and it is claimed that the total amount of solvents recovered in this industry during last year was only 9 million gal. Although comparison between these two figures

would be completely inaccurate without further breakdown, it does seem that there is at present an enormous gap between the potential and actual applications of solvent recovery. Here of course is the great challenge to adsorption within the realm of mass-transfer. Only by further extension of chemical engineering principles already successfully applied to distillation, evaporation and leaching can industry efficiently and effectively benefit from solvent recovery.

A new key to chemical literature

DR. G. MALCOLM DYSON has long been known for his enthusiasm for using mechanical aids in chemical documentation. It was this which led him to leave this country to take up a post in the research department of the American Chemical Abstracts Service. Now the first fruit of his long endeavours has materialised. It is *Chemical Titles*, the first journal in the world to be compiled by an electronic computer. It will appear twice monthly and it enables readers to keep abreast of chemical research by presenting from 2,000 to 3,000 titles from current issues of about 550 journals—110 Russian—of pure and applied chemistry. The 70 million or so operations involved in this mammoth task are performed in 25 min. by a programme written for an IBM computer and ancillary machines.

Each issue of the new journal is in two parts, the first consisting of an alphabetical index of authors together with the titles of their current papers published in the selected journals. The second part consists of a permuted title index in which the key words from each title have been arranged alphabetically down the centre line of the column. The reference code is automatically composed during machine manipulation of the data and consists of the first four letters of the author's name, his first two initials, the last two digits of the year of the original paper and the first letters of the first three significant title words. Thus under HUGGAK-60-SPI we find:

Huggins, A. K., Ottaway, J. H., Separation of a Peptide with Insulin-like Properties from Preparations of Ox-Growth Hormone, *Biochem. J.* (London), 74, 23P, 1960.

In selecting key words for alphabetisation in the permuted index the machine memory is programmed by a stoplist to ignore non-significant words such as "the," "studies," "of," etc.

Once the method of indexing has been grasped it is very easy to scan the permuted index for subjects of interest and to track down the papers in the bibliography. The cross-indexing of key words is well done and even very rapid scanning should identify the subjects in which the reader is interested.

The fact that the journal is produced by computer is a remarkable testimony to the versatility of these amazing machines. But this need not worry the reader. All he is conscious of is a first-class key to a whole world of chemical information.

The annual subscription price will depend on the

demand for *Chemical Titles* and other factors. It will probably lie between 25 and 65 dollars. Full details can be obtained from the American Chemical Society, 1115 Sixteenth Street, N.W., Washington 6, D.C., U.S.A.

Pa Perkin

THREE years ago the centenary of the discovery of mauve was celebrated and on June 17 this year 100 years had elapsed since Sir William Perkin's eldest son was born.

Regarded for a generation as Britain's leading organic chemist, William Henry Perkin junior had the run of his father's laboratory from an early age. When 17, he went to the Royal College of Chemistry before studying with von Baeyer at Munich. Perkin acted as this famous chemist's assistant for five years, and was in on some of his most valuable experiments, including work on polyacetylenes.

In 1887 he was appointed Professor of Chemistry at the Heriot-Watt College, Edinburgh, and, two years later, succeeded Carl Schorlemmer as Professor of Organic Chemistry at Owens College, Manchester. There he stayed 20 years, turning out chemists who afterwards distinguished themselves in many universities.

Perkin became an F.R.S. in 1890 and in 1912 was appointed Waynflete Professor of Chemistry at Oxford. Three years later the completion of the Dyson-Perrins laboratories there afforded him scope to complete his studies of berberine begun at Edinburgh, and to initiate a revolution in the university's attitude towards chemistry.

As the founder of a strong school of original research, Perkin left his mark upon Oxford. Clear in thought and direct in expression, he conveyed in his teaching the feeling that great problems were being conquered on the spot. Students adored him, and nicknamed him "Pa Perkin."

Among Perkin's important researches was pioneer work on rings of carbon atoms. Making rings of 3, 4, 5, 6 and 7 carbon atoms, he emerged triumphantly from controversy about the 3 and 4 rings.

Always strongly interested in complex alkaloids, he synthesised many of them, throwing light upon intricate transformations of strychnine. Practically everything known about cryptopine and protopine is due to Perkin's research, while he is justly famed for his synthesis of camphoric acid, limonene, sylvestrene, terpineol and other members of the terpene group of the constituents of essential oils.

Perkin's work on brazilin and hæmatoxylin discovered in them a protean character rivalling that of camphor, placing their chemistry upon a firm basis. Finally we are indebted to him for invaluable contributions to the dyestuffs industry both administratively and in the laboratory. He was awarded the Longstaff Medal of the Chemical Society in 1900, and the Davy and Royal Medals of the Royal Society in 1904 and 1925 respectively. He died at Oxford on September 17, 1938.



The northern aspect of the chemistry and administration blocks of the Research Laboratories in the 350 acre Alderley Park.

Seeking New Drugs at Alderley Park

By W. G. Norris

Since their research facilities were reorganised and rehoused in new laboratories at Alderley Park, Cheshire, I.C.I.'s Pharmaceuticals Division have quickened the pace of their investigations. The rate at which new compounds are being synthesised and screened has risen by 30% and now amounts to about 4,000 compounds a year. Here are some impressions of current ideas in the organisation and scope of I.C.I.'s pharmaceutical research gained during a visit to Alderley Park.

ALTHOUGH it is barely more than two and a half years since I.C.I.'s Pharmaceuticals Division moved into their research laboratories set in the 350-acre Alderley Park, already the buildings are being extended. A new block is being built to house research on pharmaceutical formulation and to provide extra office space. When this is completed the technical service departments will be centred in Alderley Park so that the whole of I.C.I.'s pharmaceutical research will be on one site.

The period since the official opening of the laboratories, in October 1957, has been used to bring the research staff up to the full establishment of some 100 senior graduates. Technical and ancillary staff bring the total force at Alderley Park to about 450. During this period the unique animal breeding unit for the production of disease-

free animals for research has been brought into full operation. As pointed out by Dr. D. G. Davey, manager of the biological group at the Laboratories in an article in the September 1959 MANUFACTURING CHEMIST, the breeding unit is now producing about 1,500 rats and 5,000 mice each week, besides a number of other small animals such as guinea pigs. The production of experimental diseases in animals is, of course, fundamental to chemotherapeutic research. The rate at which new compounds are synthesised has increased by about 30% since 1957 and is now running at some 4,000 per annum. A large and reliable supply of animals is essential for research on this massive scale and the elaborate breeding unit—sited in a 10-acre glade remote from the main buildings—is proving to be an excellent investment.

Having produced in an animal an

approximation to the human disease, the next step is to examine the response to known drugs and ensure that some reproducible and measurable effect is obtained. The stage is then set for the synthesis and evaluation of new compounds. The initial pattern may be set by the chemical constitution of drugs which are known to be in some degree effective. In this case systematic structural variations are made with the object of improving the potency or reducing the side effects. Another approach is to use biochemical knowledge on which to base a rational approach to entirely new chemical types. In entering new fields it may well be that there is no known active drug and little or no biochemical knowledge on which to base a logical programme of synthesis. In these cases the approach must be empirical, and a programme of screening is carried out based in

the first instance on the very large store of chemicals in the Laboratories' specimen collection. The procedure is to examine a wide range of chemical types until a lead is obtained which can then be pursued systematically, often on the basis of a series of working hypotheses, each of which is discarded when its usefulness is at an end. The screening is perhaps not as random as it might seem, bearing in mind that all the compounds in the specimen collection were originally made with the object of finding chemotherapeutic activity. They may have failed in their original purpose, but they remain available for new uses as knowledge advances or new ideas are generated.

Computer sorting

The specimen collection at Alderley Park has now reached the formidable total of 40,000 chemicals. Consideration is now being given to methods of automatically sorting these compounds in terms of their chemical constitution and biological activity. A study is being made of the Hollerith type of punched card system and beyond that computer coding and sorting is being considered. Among the systems which have been studied is one in which prime numbers characterise each feature of a compound so that it becomes identified by a unique product of several prime numbers. Just what system will eventually be chosen is yet to be decided, but it is clear that automatic sorting will become essential for rapid access to the vast store of information being built up both at Alderley Park and other research centres.

Method study at the bench

The objective is to free the man at the bench from as much time-wasting routine work as possible to enable him to concentrate on developing the ideas which are the life blood of a productive research department. Another innovation introduced at Alderley Park with this end in view is the application of Method Study to laboratory work. I.C.I. have for many years used Method Study to increase productivity in their factories and it is logical to suppose that it could also increase the productivity of the practical man at the bench. The intention is to devise ways in which the scientist can organise his time to the best advantage. For instance, is it feasible



Synthetic organic chemistry laboratory. In laboratories of this type several thousand substances are synthesised for biological evaluation each year.

to integrate his supervision of the half-dozen or so operations which he may be running at the bench at the same time? Can the work be dovetailed, thus reducing the attention paid to each experiment and freeing the scientist for other creative work? Results obtained so far suggest that Method Study can increase productivity in the laboratory just as it can in the factory.

New research trends

When I.C.I. entered the drug industry in 1936 they followed the German pattern in evolving chemotherapeutic research from their experience in synthetic organic chemistry. The genesis of the present Pharmaceutical Division was an eight-man team which comprised the new medicinal chemicals section of the Dyestuffs Group at Blackley, Manchester. An early success of this group was *Sulphamethazine*. Synthetic organic chemistry is still the basis of research at Alderley Park, but now attention is being given increasingly to biologicals.

I.C.I. have not yet produced vaccines, but it is significant that the company is now concerned in the development of interferon—they, Burroughs Wellcome and Glaxo are collaborating with the Medical Research Council to produce large supplies of this interesting anti-viral substance. However, current thinking on interferon at Alderley Park is

that it will be a long time before it becomes a practical means of virus therapy.

The large-scale manufacture of most I.C.I. pharmaceuticals is carried out by other divisions of the company, principally the Dyestuffs Division. *Fluothane*—the successful inhalation anaesthetic developed in 1952—is made by the General Chemicals Division at Widnes. In 1953 the production facilities of the Dyestuffs Division were supplemented by a bulk medicinals plant at Grangemouth, Scotland, and here, for instance, the manufacture of *Sulphamethazine*, *Paludrine* and *Mysoline* has been concentrated. Processing of pharmaceuticals into ampoules, tablets, creams, lotions and powders is carried on at the Pharmaceutical Division's factory at Linlithgow.

Cancer and viruses

One-fifth of the research effort of the Pharmaceuticals Division has for a long time been devoted to long-distance research, particularly on cancer and the smaller viruses. It is now recognised that cancers and viruses have much in common. When a virus invades a cell it becomes part of the cell, begins to organise it and causes it to "run wild." A cancer cell is also a "wild" cell, so that it has a strong resemblance to a virus infected cell. In animals—but not yet in humans—there is evidence that viruses cause a

condition that can only be called a cancer. How are cancers induced? Is it a failure of an inhibitor or a regulator in the body?

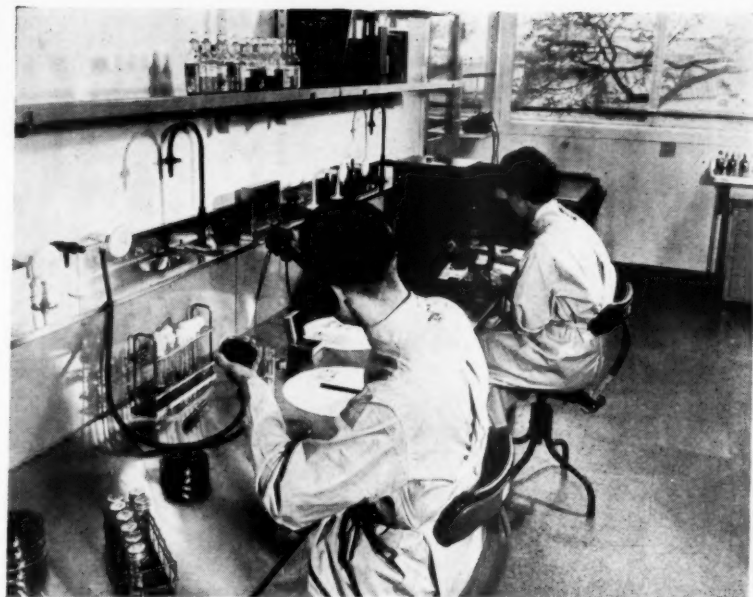
So far the most notable product in this field in which the company is interested is *Tretamine* (triethylene melamine), which was originally made in Germany for a totally different industrial purpose. This drug was recently used in Manchester for the treatment of lung cancer in a series of 43 patients of which 30 showed some improvement. It is a very powerful drug and the surgeon, Mr. David Jack, had to use penicillin and other drugs to avert the risk of damage to the marrow and blood cells.

The virus problem is not made easier by the rapid discovery of new viruses. In the last two years over 200 new viruses have been found. It is a question not only of finding the viruses that cause diseases but of finding the diseases caused by newly isolated viruses.

Research is being enormously aided by the invention of methods of growing viruses outside the human and animal host, as, for example, the recently announced discovery of the Medical Research Council's Common Cold Unit of the successful culturing of at least one common cold virus in embryonic tissue.

Veterinary research

Like many companies, I.C.I. are deeply concerned in the growing



Bacteriology laboratory. In the study of the effect of antibacterial agents on the micro-flora of the throat, many cultures are prepared for microscope examination.

market for veterinary medicines and chemicals. Phenothiazine, now the most widely used drug for worm infestation, was first made in Britain by I.C.I. An outstanding recent product is *Helmox* (cyanacetyhydrazide) which cures husk or lungworm in cattle, sheep and pigs. *Hibitane*, the general purpose antiseptic, is now widely used to control mastitis.

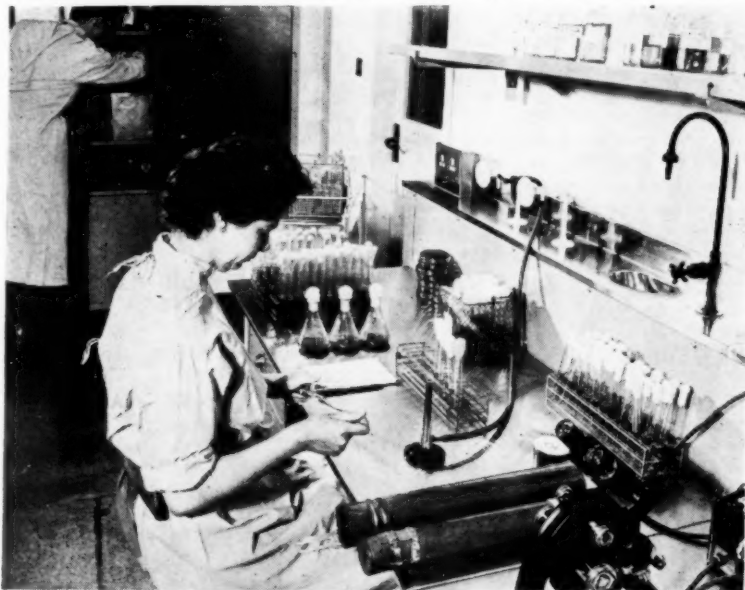
Then there is *Antrycide*, the trypanocide which has proved so useful in Africa.

The bias of current veterinary research is still towards the major veterinary problem—worm infestation. Among the projects in progress is an attack on liver fluke. Some elegant experimental techniques are being employed to develop compounds active against this scourge of livestock.

It is refreshing to visit Alderley Park as it enters its fourth year of operation and to find such a wealth of enthusiasm, intellectual ability, technical skill and equipment concentrated on problems of chemotherapy. These magnificent laboratories are a national asset. When they were opened it was stated that they had cost £1.5 million to build and equip and that the research budget was running at half a million pounds a year. Since then it is certain to have been increased and it must account for a substantial proportion of the £5 million odd spent by the British pharmaceutical industry on research last year.

As already mentioned, the number of new compounds being synthesised and screened is steadily rising. On the other hand, the number of development projects—40 when the laboratories were

(Continued on page 300)



Bacteriology laboratory. Stock cultures of many different species of bacteria are maintained in the bacteriological laboratory.

Changes in Pharmaceutical Production

Trends in Methods and Machines

By E. K. Samways,* B.PHARM., B.SC., F.P.S., F.R.I.C.

Mixing

The mixing of powders, pastes and liquids is a fundamental of pharmaceutical production. Although a trough mixer for dry powders will probably always have its place, it is undoubtedly yielding to double-cone and rotary cube type mixers. These two types are efficient and relatively trouble free. Their only limitation is the ultimate discharge of the mixed material. Where dry powders have to be sifted, the traditional method of batch sifting in boxes shaken by overdriven mechanical shaking machines has almost given way to either the rotary sieve or the vibratory sieve, both of which can be operated continuously. There is need to follow grinding and sifting machinery with metal detectors or magnetic collectors; where magnetic materials are unsuitable or not available, the electronic metal detector is now standard equipment in many branches of the pharmaceutical industry and I think there will be many production men who share my surprise, not so much at what their detector occasionally finds as what their customers of yesterday failed to notice.

Just as trough mixers are losing ground for powder mixing, for paste mixing they are being replaced by the sun-and-planet type of bowl mixer, which does not suffer from leakage of lubricants through the glands: one modification uses a flat-bottomed vessel in which a flat-ended blade revolves eccentrically. The bowl type of mixer, either with the hemispherical or the flat-bottomed vessel, is now available with very large power inputs and with interchangeable bowls on wheels or on dollies, and is more easily cleaned than the traditional paste mixers which I knew in the days when lozenges, for example, were more popular than they are today.

Of all mixing problems, liquid mixing perhaps has had most study in recent years because of the importance of mixing and aeration in fermentation vessels. Where a piece of equipment is specially designed for a single operation, the chemical engineer can make it extremely efficient. Where, however, a tank and a stirrer are used for a variety of operations, a little attention to sensible disposition of baffles, to the position of the propellers and to the adequacy of power input is always worth while.

Granulating and drying

Except for small runs, the traditional method of granulating by pressing through a sieve is yielding place to the high-speed granulator which makes use of a hammer mill to force pellets through a sheet of perforated metal. These mills are now offered in several forms by at least two British manufacturers and are generally excellent for moist granulations, and I foresee considerable extension in their use.

The rotary kiln has never found much employment in the pharmaceutical industry and the belt dryer on which material is heated by infra-red or high-frequency induction heating, has not so far been widely adopted. Tray

dryers are still widely used, but I think that there will be changes in the drying of granules. The tray made of a wooden frame filled in with wire netting and lined with paper has long since given way to either the enamelled iron or the aluminium tray, and these are now giving way to plastic trays. But I believe that tray methods, with all the handling involved, will give way either to the high-frequency-heated tunnel dryer or more probably to the floating bed type of dryer. Formerly devices for drying solids in continuous currents of air have either been too cumbersome for the pharmaceutical industry or unsuitable because the attrition between particles produced an excess of fine material. There are signs that some of these problems are now being overcome and the drying of granular materials, including tablet granules, by a continuous or semi-continuous method using a current of hot air in a tower, will, I foresee, be developing during the next few years.

Tablet compressing and coating

New agents have become available in recent years to help the tablet maker, notable examples being the carbowaxes, finely divided silica, and modified starches: other additions can be expected.

Major changes have taken place in the design and operation of tablet compressing machines, where improvements in robustness and quiet operation have gone on side by side with the achievement of higher production speeds. Performances now achieved would have sounded fantastic a few years ago; high-speed rotary machines now produce 300,000 tablets per hr.

The layered tablet keeps separate ingredients which should be segregated and one has the choice of concealing the separation by similarly colouring both halves or of accentuating it by using contrasting colours.

The use of tablets is increasing but many active substances need to be covered up. The compression-coated tablet, with similar advantages to the layered tablet, has most of the advantages of the pan-coated product while being easier and quicker to produce within specification. The traditional art of pan coating, however, is yielding to work study and the application of mass production techniques. There now exist fully automatic coating plants using conventional pans in which the tablets are alternately sprayed with the warm syrup and dried with warm air, the whole operation being controlled electrically from a console.

Sterilising

Sterilising operations, whether by wet or dry heat, have for some time been automatically recorded, for it is quite simple to equip an autoclave or oven with a temperature or pressure recording device operated by clockwork or electricity. However, the industry has been rather slower to adopt the recorder-controller so popular in the chemical industry. Autoclaves now available complete a predetermined cycle automatically and will be used increasingly in pharmaceutical production. The automatically controlled dry heat steriliser is also

* Director, Allen and Hanburys Ltd. Extracted from an address to the Pharmaceutical Society, London.

available and becomes increasingly useful as realisation grows that an extra cycle can be obtained in the hours of darkness with no attendance whatever. A further refinement, although of somewhat limited use in the industry, is the acceleration of sterilising cycles by artificially cooling the contents of the steriliser. In hot-air sterilisers this can be done with a supply of cold sterile air, and with solutions in sealed bottles in an autoclave by spraying them with a mist of water in such a way that the heat of evaporation of the water droplets is derived from the containers with considerable lessening of the time necessary to bring the contents of the autoclave to a point at which danger from superheat is completely removed.

Packaging operations

Where the lay person seems to think that almost any process can be speeded up by merely driving the machinery faster, most of us are well aware that limitations of viscosity, the volume to be filled and the nature of the liquid make the speeding up of pharmaceutical filling anything but simple beyond a certain point. With small ampoules the neck size affects the needle size and the highest rate with common materials that can be obtained with a single needle fill is around 25-30 ampoules a min. Two-needle, two-stage machines, and more recently three-needle, three-stage machines, are available, giving speeds rather better than 100 per min., although a new American machine has been described giving speeds on small ampoules of 150 per min. An interesting bottle filling device that has recently come within my knowledge is one which measures the delivered volume with sufficient accuracy by opening an orifice full bore for a precisely measured length of time. This time is controlled electronically and permits the filling of litre bottles at the rate of 16 per min. with a clean liquid cut-off and allowing, of course, time for mechanical transfer of the full bottle away and an empty bottle into the filling station. This device is accurate within 2% and I see no reason why this principle should not be extended in use.

The balanced production line is coming into increasing use for many pharmaceuticals. The type of line with which we are all familiar has bottles fed on to it mechanically, or by hand, and provides filling, capping, labelling and cartoning stations. In many cases these stations are manned by an operator, but here, too, the scene is changing in favour of the automatic filler, followed by the automatic capping unit, the in-line labeller and the automatic cartoner, to provide a packaging line capable of up to 180 packages per min. with the container untouched by hand from the time it enters the belt to the time it leaves in its cartoned form for outerling or casing. Until recently a single breakdown at any stage on such a line led to the halting of the full line. A tendency which began on the Continent is now appearing in this country, namely that of interrupting the packaging line with an accumulator table at one or two positions in its length so that failure at one stage does not necessarily involve hold-up at all stages along the line.

High-speed operation has brought with it the need for much greater control of the materials being handled. Normally pharmaceutical products are of constant characteristics, but bottles and cardboard, for instance are much less so. If full advantage is to be taken of high-speed operation, machine change-over time and machine down-time must be curtailed by minimising the range of shapes and sizes of pack and by standardising the items

in the selected range within narrow tolerances. Bottles, for example, need controlling for weight, capacity, height, body and neck diameter and neck ovality; tubes for length and ovality; cartons for caliper of board and direction of grain; plastic and metal items for flexibility or hardness.

Plastics

Plastic closures have made way for the complete plastic container and even if plastic tubes have as yet only a small following, flexible bottles are becoming increasingly used and the sachet type of presentation, already familiar in the toilet field, is beginning to invade the pharmaceutical. Plastic films are already much in evidence as packing materials for tablets in the strip presentation, although considerable further work is yet required, both on the machines to avoid the risk of occasional perforation and on foil and film materials to deal with problems of channelling and of permeability to water vapour.

Plastics of low toxicity, similar in composition to those used in the food industry, have recently been adopted for the presentation of injectables, transparent p.v.c. tubing having for some time supplanted rubber for intravenous injection sets. More recently high density polythene and a special grade of nontoxic p.v.c. have been developed for containers for the intravenous injection solution itself. To the best of my knowledge even high density polythene containers are not entirely satisfactory when autoclaved, but careful attention to autoclaving techniques permits the use of selected p.v.c. in the production of a unit which can be sterilised by autoclaving after first having been filled, sealed and connected with the giving set. Similarly, a plastic bag containing an anticoagulant is available for the taking of human blood and for its subsequent administration or conversion to plasma. A number of companies in Europe and America are working on development projects in this field and extensions of this use of transparent plastics can be expected.

Materials of construction

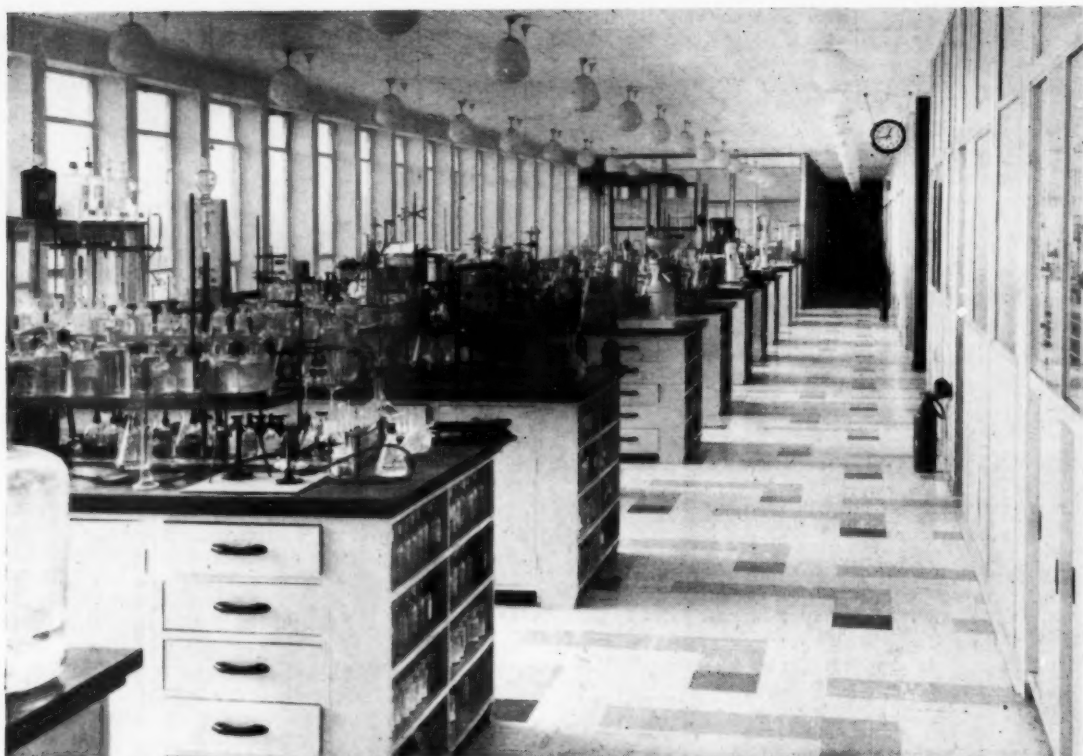
The traditional copper vessel, internally tinned more or less completely with approximately pure tin, has now almost given in to the onslaught of stainless steel, but other materials deserve mention.

Teflon for gaskets, seals and bearings becomes more available every day and is less inclined than some plastics to become charged with static electricity.

Pyrex glass flasks up to 100 litres in size, Pyrex condensers of 60 sq. ft. and Pyrex glass pipelines are almost commonplace. In association with this equipment there is a growing use of resin-bonded asbestos laminates for stopcocks. This same material appeals to an increasing number of chemical and pharmaceutical manufacturers for drying trays, stirrers and other items on account of its chemical resistance, physical strength and relative lightness.

Rigid and semi-rigid p.v.c. makes excellent fan casing and trunking: jets which stand steam sterilising can be made with Teflon or with resin-bonded asbestos laminates: and bench tops which are hygienic and pleasant to work on can be cheaply prepared with plastic laminates like Waverite or Formica. Colour contrast between work and background is often helpful and benches with coloured plastic tops have been found helpful.

(Continued on page 310)



The main open area of the laboratory, airy, bright and colourful. The double benches are 4 ft. x 14 ft.

£100,000 a Year for Research on Hair Cosmetics

County Laboratories Ltd. employ 62 people, including 22 graduates, in their new Products Research Laboratory and spend about £100,000 a year to keep themselves ahead in hairdressings like "Brylcreem" and "Silvikrin," and in shampoos and other hair cosmetics.

THE NEW Products Research Laboratory of County Laboratories Ltd., at Brentford, Middlesex, is an object lesson in making the utmost use of expensive space. It occupies the second (top) floor of the new County building on the Great West Road and it measures 230 x 40 ft. This gives a little more than 9,000 sq ft. of floor space and in this relatively small area a staff of just over 60 work in comfort. This has been achieved by making most of the laboratory an open area so that no space is wasted on corridors. The main area accommodates nine double benches (4 ft. wide x 14 ft.) and two single benches at either end. There are no shelves over the benches, so the working area remains light and unobstructed. Glassware is stored in cupboards

with sliding glass doors fitted at the side of the laboratory. The effect is airy and open, with bright colours, plenty of windows and intensive lighting (lamps, not fluorescent strips). The ceilings are sound absorbent and the floors are plastic tiles.

County's products

Airiness, lightness and cleanliness—these are the first and abiding impressions of the new laboratory. What does it do? It carries out continual study of County's products to ensure that quality is maintained and improved whenever possible and that new products are ready for marketing when commercially desirable. These products are hairdressings and shampoos and, lately, toothpaste (*Macleans*). If this seems

a narrow range of products to occupy 62 people, it should be remembered that County (a Beecham Group company) hold 80% of the hairdressings market in Great Britain and a third of the shampoo market. The business has grown fast in the past few years, from a turnover of £1 million p.a. to something like £7 million. These are ex-works prices. After purchase tax and wholesaler's and retailer's margins are added the consumer probably pays twice as much. If overseas business is added the total ex-works figure is about £14 million.

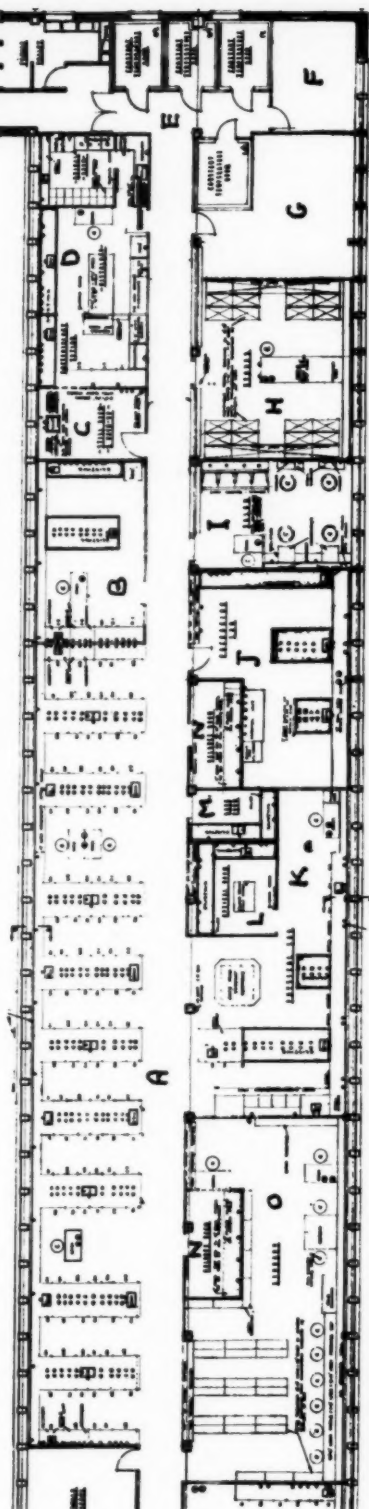
The biggest single product is *Brylcreem*, a mineral oil hair cream. The new factory at Maidenhead is now turning out about 30 tons of *Brylcreem* every working day. Taking

COUNTY LABORATORIES' PRODUCTS RESEARCH LABORATORY, BRENTFORD, MIDDXX.

A. Main Laboratory for Analysis and Formulation.
B. Biochemistry.
C. Wash-up.
D. Physiology, Histology and Bacteriology.

E. Constant Temperature Rooms—1°C., 20°C., 30°C. and 40°C.
F. Inspection Room for Stored Samples.
G. Spare Room.
H. General Stores.
I. Salon.

J. Packaging.
K. Physical Chemistry.
L. Optical Dark Room.
M. Photographic Dark Room.
N. Balance Rooms.
O. Library.



overseas production as well, this works out to about 1 cwt. of *Brylcreem* being used every minute. Although a basically simple product, it has to be carefully formulated to ensure uniform quality wherever and whenever it is used.

Sight, smell, touch

The Director of Research, Dr. Robert H. Marriott, a well-known cosmetic chemist, impresses on his staff that what matters is what the consumer sees, smells and feels when he or she uses a product. First and foremost great care is taken with raw materials. Products Research set standards that have to be applied in all factories. When a product is ready for marketing, all the information is passed to the Quality Control Laboratory, which is independent of Product Research, and which employs the standards set by Dr. Marriott and his staff.

The heart of the laboratory is the formulation department. This department has to understand the chemical and physical properties of a wide range of substances. Cosmetics have to be looked at from many angles. First of all they have to be put on the living skin, so the histological structure and biological function of the skin must be well understood. There is a small animal section where the effects of cosmetics on mice can be studied. Skin sections are studied with a Beck binocular microscope fitted with apochromatic lens, magnification $\times 1,400$.

As cosmetics are essentially personal things they must have an appearance, odour and texture pleasing to the greatest number of people. An outstanding example of an extremely popular cosmetic is *Brylcreem*, but such wide appeal is not possible with shampoos. Accordingly a number of different shampoos are produced to cater for the widest possible range of tastes.

Storage tests

All products have to withstand the rigours of long-term shelf storage. Even with quick-selling lines there may be the odd packet, jar or tube that gets pushed aside and it may be two years before it is sold. The bacteriology department takes care of such things as anti-oxidants and preservatives. The final test is storage at different times in four separate rooms which are kept at constant temperatures, one just above freezing (1°C.), another at 20°, another at 30° and the fourth at

40°. By storing products in their final packages in these rooms and alternating between hot and cold to simulate the diurnal changes of temperature, a good idea of the stability of a product is obtained. If a product fails the formulator has to find the reason why and modify the formula or manufacturing process accordingly.

In this connection packaging problems have to be considered. The Packaging Department examines and tests all packaging materials for the fitness for purpose and sets standards against which the Buying Department and the factory purchases packaging. Among the equipment in the Packaging Laboratory is an aerosol filling unit for experimenting on such products as *Bristow's Star Spray* hair set. There are three recording balances to check changes in weight during storage, and a humidity cabinet.

Unusual equipment

As will be gathered, no expense has been spared to equip the laboratory with the best possible instruments and apparatus. There is a Shandon liquid vapour-phase chromatography unit for analysing perfumery and essential oils, and to try to follow changes occurring in storage. This apparatus is so sensitive that it can be upset by the background odour present in the laboratory but imperceptible to the human nose.



Two space-saving ideas. Left: Wall cupboards with sliding glass doors for storing glassware. These run along one side of the laboratory and free bench space for maximum utilisation. Right: Sliding storage shelves in the laboratory store make full use of confined space and give instant accessibility to stores.



The new County Laboratories building on the Great West Road, Brentford. The Products Research Laboratory is on the top floor.

Another useful apparatus is a fadeometer or artificial sunshine cabinet. This can produce the effects of a brilliant June day in about 10 hr. and it determines the stability to sunlight of all products, including the stability of the labels. It is a circular cabinet with a xenon arc source. This gives a longer spectrum than natural sunshine, but unwanted waves can be cut out by a jacket containing a solution of copper sulphate in water; this acts as a screen and cooling jacket at the same time.

There are many other pieces of apparatus, some common to most laboratories and others peculiar to cosmetics research. For instance, there is an adaptation of the glossmeter used in paper laboratories with which it is hoped to find a physical means of assessing the gloss on hair. Then there is an instrument for measuring the elasticity of hair before and after shampooing. There is a Geiger counter for radioactive experiments, a fully recording spectrophotometer, a polarimeter and many other instruments all devoted to organic chemistry and the special problems of hair cosmetics.

One facility in the laboratory is unique. This is a hairdressing salon run by highly qualified hairdressers.

Over 500 men and women participate in research panels which provide chemists with a wide variety and condition of hair for testing products.

Finally, there is the pilot plant for making small batches of products for testing. This is housed in a separate building and it is equipped with vacuum mixers (toothpaste is mixed under vacuum to exclude air and its corrosive effects on tubes), triple roll mill, refrigerator, heat exchanger, heat sealer for plastic sachets, etc.

County Laboratories spend about £100,000 a year on product research and the new laboratory cost an equal amount to build and equip. Mr. Robert Murphy, the managing director, takes a keen interest in the new laboratory, recognising its essential rôle in upholding the reputation of County products.

Aspects of the Chemotherapy of Cancer—2

By Walter Davis,* Ph.D.

In this second part of his article, Dr. Davis deals with anti-metabolites, purine antagonists, folic acid antagonists, pyrimidine antagonists, amino acid antagonists, antibiotics and hormones.

Mechanism of action

The first part of this article (June, p. 233) described four groups of compounds — the dichloroethylamines ("nitrogen mustards"), diepoxides, the di- and tri-ethyleneimines and dimethanesulphonates — from each of which has come some compounds that exert similar though by no means identical effects on experimental tumours, on normal blood, and on the blood and lymphatic system of leukaemic patients. What are their common features? Firstly: they are all alkylating agents, and in these reactions it is possible to postulate, in each case, a reactive unstable intermediate, the carbonium ion (Fig. 18). This carbonium ion might then react at an available electron-rich centre in normal tissue. Secondly: they are all bifunctional. Thirdly: as has been explained for Myleran, the two functional groups should be an optimum distance apart. This applies to the diepoxides, where increasing chain length was found to be accompanied by decreased biological activity, and also to the nitrogen mustards, where separation

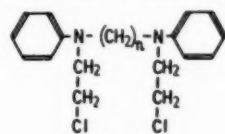


Fig. 19

of the two chloroethyl groups by attachment to separate nitrogen atoms (Fig. 19) gave inactive compounds if the inter-nitrogen distance was greater than four methylene groups' length.²⁸ (Degranol, Manitol Myleran and Nonane appear to be exceptions.)

It is logical to look for a mechanism of action that involves as many of these three similarities as possible.

In vitro experiments have demonstrated alkylation under physiological conditions of temperature and pH, of carboxyl groups,^{29,30,31} amino groups,³² sulphhydryl groups³³ (but only at pH values higher than physiological) and phosphoryl

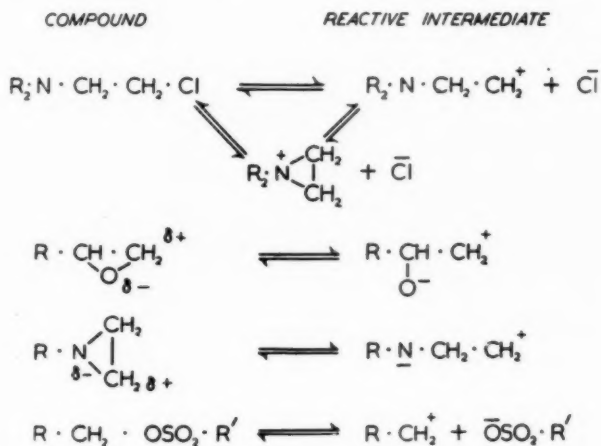


Fig. 18

groups.³⁴ (There is some reason for believing that SH-groups actually *in situ* on a protein surface, might well be more reactive at physiological pH, than the individual thiols that have been studied *in vitro*.) All these groups are of course present in considerable numbers in nucleoprotein and general cell constituents, but attempts to demonstrate alkylation *in vivo* have only shown unambiguously that sulphhydryl groups and purine ring nitrogen atoms can be involved.

The alkylation of sulphhydryl groups was established by most elegant studies using the combined techniques of autoradiography and

paper chromatography.^{36,37} A male Wistar rat was injected with Myleran labelled on the 2 and 3 positions with the radioisotope carbon-14. Autoradiographs of paper chromatograms of the rat's urine collected during 24 hr. after injection revealed one major metabolite. After very painstaking studies this was finally identified as 3-hydroxytetrahydrothiophene-1,1-dioxide, derived from the cyclic dialkylation of the sulphhydryl group, in cysteine for example, by Myleran followed by a metabolic dethiolation, oxidation and hydroxylation (Fig. 20). Thus, in one set of experiments, the involvement of all three features of the alkylating

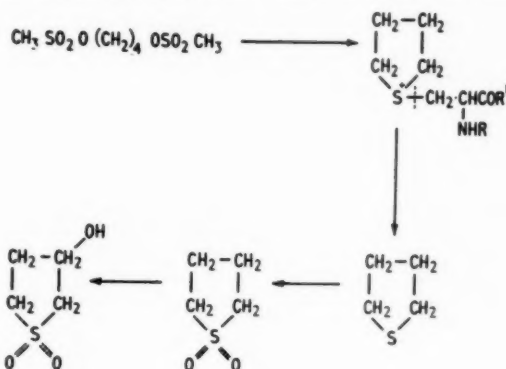


Fig. 20

agents has been demonstrated—alkylation, bifunctionality, and the need for an optimum distance between the two alkylating arms to achieve cyclisation.

Experiments in which HN2 labelled with carbon-14 was administered to rats showed that alkylation was associated with the purine fraction of both ribo- and deoxyribonucleic acid.³⁸ A recent extension of this work with sulphur mustard labelled with radioactive sulphur-35, has by using similar techniques to those just described shown the major radioactive metabolite to be 7-(β -hydroxyethylthioethyl) guanine.³⁹ Thus one arm of sulphur mustard had alkylated guanylic acid nucleotide on the ring nitrogen (7-position) and the other arm had hydrolysed. Alkylation of the purine in the 7-position then made the linkage with the ribose phosphate moiety less stable and the alkylated purine was split off (Fig. 21). These experiments therefore only demonstrated the involving of the prime feature, alkylation, of these drugs.

These studies, one showing alkylation of sulphhydryl groups in protein or peptide, the other showing the purine ring-nitrogen in nucleic acid as the target of alkylation, are of course not mutually exclusive, neither do they exclude the possibility of yet other sites being alkylated *in vivo*. Esterification of carboxyl or alkylation of amino groups in protein may also take place, as might the esterification of phosphoryl groups in nucleic acid. Indeed much work was done to establish the existence of this last reaction, but the results were ambiguous and could equally well have been interpreted as showing ring-nitrogen alkylation or phosphate esterification. No isolation of esterified phosphate has been achieved, perhaps because the resulting phosphate triesters would prove too unstable.^{40,41}

The question that still remains to be answered is which of the reactions that have been firmly demonstrated as occurring in the living animal—or any others that may be postulated—are significant in producing the multiplicity of biological effects of which the alkylating agents are capable. Histological examination of tissues from animals that have been treated with the alkylating drugs very often reveals marked abnormality in the chromosomal patterns of divided cells. In fact the

name “mitotic poisons” was given at first to the alkylating agents. Genetic study of fruit fly, *Drosophila melanogaster*, after injection with alkylating agents establishes patterns of induced mutations, which implies interference with the hereditary material located on the chromosomes.⁴² Male rats to whom alkylating agents have been administered develop a transient sterility which is interpreted as interference with spermatogenesis.⁴³ *Haemophilus influenzae* transforming principle which is almost pure nucleic acid is extremely sensitive to nitrogen mustards and is inactivated by the DL-isomer of Melfalan at a concentration of 10^{-4} M.⁴⁴

As by far the largest part of the mature spermatozoa is nucleoprotein and as this is also the basis of chromosome structure, these four biological effects just described all lend support to the theory of alkylation of nucleic acid as the biologically significant reaction. There is additional chemical evidence to be considered. Alkylation of a nucleotide purine, as has been already noted, leads to the splitting off of the purine from the ribose phosphate through which it is linked in the nucleic acid macromolecule.⁴⁵ This in turn leads to instability of the bond between the ribose and the phosphate. If this bond breaks then the nucleic acid chain molecule is ruptured at that point. Thus the reaction of only one alkylating molecule would appear to be capable of disrupting a nucleic acid molecule whose molecular weight is more than 1 million. This perhaps explains why these drugs, which appear to alkylate more or less indiscriminately throughout the body, are nevertheless capable of inhibiting the growth of an experimental tumour at doses

of a fraction of a milligram per rat.

Viewed in this light, the argument for the dethiolation reaction is less strong. Because of the rapid turnover of thiol groups in protein and the relatively large amounts available for reaction, it would seem that rather larger doses would be needed if this were the significant reaction. Glutathione, which has been shown to be dethiolated by Myleran, is a growth factor and its inactivation would have a profound effect, but again larger amounts of the drugs would be needed than have been shown to be necessary for biological effectiveness. There might of course be a specific SH-containing enzyme present in only very small amount and involved in a vital stage of the metabolism of cell growth, that is being inactivated, but this is sheer speculation.

However, it is perhaps unwise to compare these two mechanisms, seeking to establish one of them as the general mechanism of effective alkylation at the expense of the other. Alkylation of purines has not yet been demonstrated with dimethanesulphonates, neither has dethiolation been achieved with nitrogen mustards.

Indeed there is cytological evidence that points to two different mechanisms for these two series. Cells in tissue that has been treated with Myleran exhibit a marked lengthening of the interval between each mitosis, so that the effect is one of very slow growth.⁴⁶ Nitrogen mustards tend much more to achieve growth inhibition through cell death. Further, since the premitotic period is associated with a build-up of available SH-groups in the cell, their alkylation might well result in the observed delay of mitosis.⁴⁷

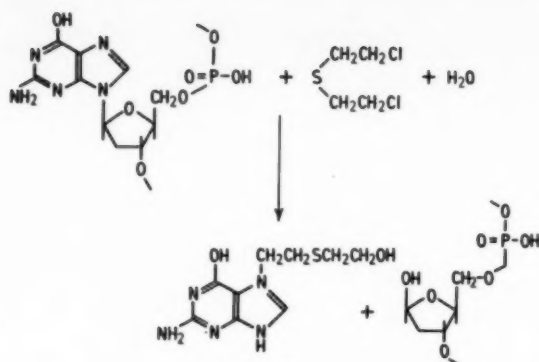


Fig. 21

The anti-metabolites

The biochemistry of growth, both normal and malignant, involves above all else the rapid synthesis of nucleic acids in large amounts and with accurately reproduced structure. The possibilities of interfering with this process at one or more of many possible points in a complex mechanism have been exploited in the large groups of potential anti-tumour drugs known as anti-metabolites.

The biosynthesis of the nucleic acids, both DNA and RNA, involves the synthesis of the purine and pyrimidine bases linked to ribose- or deoxyribosephosphate and then the polymerisation of the nucleotide units in their correct order to give the polynucleotide chain with a molecular weight of say 6×10^6 for DNA and 3×10^4 for RNA. The building up of the polymer, with the bases appearing in their correct order, seems to be the job of specific protein structures present in the cell which transmit the essential information. Such a complex pathway obviously offers many possibilities of throwing spanners into the works. Most effort has been concentrated on putting anti-purines and anti-pyrimidines into this system in the hope either that their incorporation into nucleic acid would produce a "fraudulent" molecule incapable of fulfilling its required functions, or else that their presence would competitively inhibit the incorporation of the normal purine or pyrimidine and so hold up biosynthesis at that point. Whichever mode of action prevailed, the result should be growth inhibition.

Purine antagonists

The purine bases present in nucleic acid are adenine (Fig. 22, I) and guanine (Fig. 22, II), and many

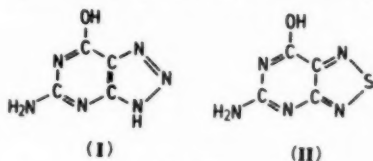


Fig. 22

analogous compounds have been made and tested as purine antagonists. These fall into three main groups. Firstly there are those compounds in which the substituents in the 2 and 6 positions have been changed. 2 : 6-Diaminopurine (Fig. 23, $R_1=R_2=NH_2$) was one of the

first biologically active compounds synthesised, being able to antagonise adenine in *Lactobacillus casei*.⁴⁸ 6-Mercaptopurine (Fig. 23, $R_1=SH$, $R_2=H$) has similar activity, and also strongly inhibits the growth of an experimental tumour in mice. So, too, do 6-chloro- (Fig. 23, $R_1=Cl$, $R_2=H$) and 6-methylpurine (Fig. 23, $R_1=CH_3$, $R_2=H$).⁴⁹ Purine itself is also a tumour inhibitor. Many other mono- and disubstituted purines have been tested,⁵⁰ but of them all, only 6-mercaptopurine (Purinethol) has been of value in clinical application, where it is widely used in the treatment of acute and chronic myelocytic leukaemia.⁵¹

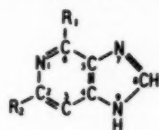


Fig. 23

In the second group of purine antagonists are derivatives of 6-mercaptopurine and 6-chloropurine in which the 9-position is also substituted by an alkyl group. Compounds of this type where the 9-alkyl substituent is ethyl, *n*-butyl and cyclopentyl are all active inhibitors of experimental tumours, but their therapeutic index is lower than the parent 6-mercaptopurine or 6-chloropurine. This is of interest since it has been shown that these purine antagonists appear to be rapidly transformed into their ribotides very soon after administration and this of course involves a linkage in the 9-position.^{52,53}

The third group is comprised of compounds in which the position of the ring-nitrogens is changed (for example, the pyrazolopyrimidines) or additional hetero-atoms, either N or S, are included. Examples of this type are 8-azaguanine (Fig. 24, I)⁵⁴ and its thiapurine analogue (Fig. 24, II),⁵⁵ both active as anti-purines and against experimental tumours but offering no clinical advantage.

The folic acid antagonists

An essential rôle in the biosynthesis of purines is played by a derivative of folic acid (Fig. 25, $R'=OH$, $R''=H$) known as the citrovorum factor. Antagonists that block the conversion of folic acid into citrovorum factor (folinic acid) (Fig. 25, $R'=OH$, $R''=CHO$) or antagonise folinic acid itself will inhibit purine synthesis and are potentially growth inhibitors. Out of a very long series

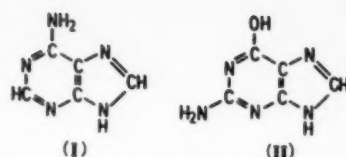


Fig. 24

of compounds related to folic acid, two have been found useful in the treatment of acute leukaemia especially in children. These are called aminopterin (Fig. 25, $R'=NH_2$, $R''=H$) and amethopterin (Fig. 25, $R'=NH_2$, $R''=CH_3$), also known as Methotrexate.^{56,57} This latter drug, which has the disadvantage that it eventually induces drug resistance, is used often in combination therapy with 6-mercaptopurine to overcome this limitation.

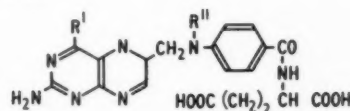


Fig. 25

Pyrimidine antagonists

The synthesis of anti-pyrimidines had not led to any drugs that held out promise as anti-tumour agents until the relatively recent syntheses of 6-azauracil^{58,59} and 5-fluorouracil.⁶⁰ This work followed the finding that tumours incorporate more uracil into RNA than does normal tissue, and both these drugs were found to inhibit experimental tumours and to be incorporated into intact nucleic acid, though it is doubtful if this is involved in the mechanism of tumour inhibition.⁶¹ 5-Fluorouracil seemed promising enough for clinical trial, but although it brought some occasional benefit, it was extremely toxic.⁶²

Amino acid antagonists

In the *de novo* synthesis of nucleic acid in the living cell the amino acid glutamine (Fig. 26, I) is essential for

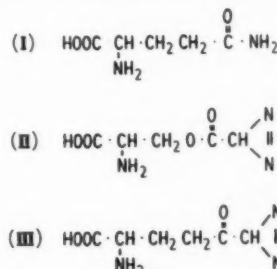


Fig. 26

the introduction of amino groups in at least three stages of the process and its inhibition must profoundly affect cell development.⁶³ Two antibiotics that were found to be tumour inhibitors were found to act by glutamine antagonism. These are *L*-azaserine (Fig. 26, II)⁶⁴ and DON (6-diazo-5-oxo-*L*-norleucine) (Fig. 26, III).⁶⁵ Their clinical trials were rather disappointing for there were rare and random instances of favourable effects, but overall the results were quite inconsistent.

These two compounds are nevertheless very interesting. Whilst it is obvious that their activity depends on their structural similarity to glutamine, the terminal diazo group, nevertheless, is potentially capable of releasing an alkylating carbonium ion.

Another alkylating agent that appears to act as an anti-aminoacid is the dichloroethyl derivative of carbamoylserine (Fig. 27).⁶⁶ It was

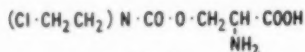


Fig. 27

at first thought that this drug, which was an active inhibitor of experimental tumours, was another example of a "latent activity" mustard in which the molecule broke down to give serine and the active dichloroethylamine. Biochemical studies have shown, however, that the drug appears to antagonise the incorporation of serine by an experimental tumour.⁶⁷ Upon which part of its character—alkylating agent or anti-metabolite—activity depends is not yet known.

In the search for potential growth-inhibitors among derivatives of the aminoacids, α -substituted compounds seemed a likely line to follow. This in turn led to the synthesis and examination of a series of cyclo-alkane amino-acids, extending from the α -aminoacid of cyclo-propane up to the one derived from cyclo-octane.⁶⁸ One compound alone out of this series, the cyclopentane amino-acid (Fig. 28), proved to be



Fig. 28

biologically active and capable of inhibiting experimental animal tumours. Its two glycine peptides were also found active.

The only other anti-amino-acid that has been reported as a tumour

inhibitor is *DL*-ethionine, which is an antagonist of the naturally occurring methionine.⁶⁹

The antibiotics

The search for new antibiotics has reached vast proportions in the pharmaceutical industry, and, especially in America, attempts are made to screen every new bacterial fermentation product as a potential anti-cancer drug. Azaserine and DON, already described, come from this source, being derived from *Streptomyces*. The group of actinomycins have been very closely studied,^{70,71} and of them Actinomycin D has proved to be of clinical value when combined with radiotherapy.⁷² Certain tumours, such as rhabdomyosarcoma, are known to be radiation resistant, but after intravenous administration of Actinomycin D, radiation produced impressive temporary regressions.⁷³ It is however very toxic and the search for active but less toxic analogues is being pursued both synthetically and biologically.

Two Japanese preparations, Mitomycin C and Sarkomycin, have been reported active,⁷⁴ but these results have not been substantiated by clinical trials in America.⁷⁵

Hormones

In the introduction reference was made to the rôle of endocrine dysfunction in tumours at sites normally associated with hormonal activity like the breast, uterus and prostate. Hormone chemotherapy applied to these cancers has met with some success, but it is difficult to extract a clear pattern from the great variety of different clinical applications that have been reported. There is a broad generalisation, that the application of male hormones—androgens—have been of value in the treatment of breast cancer in women, and conversely, female hormones, oestrogens, are effective for cancer of the prostate in men. The latter case, prostate cancer, is really the only good example of a solid tumour responding well to chemotherapy. Stilboestrol is the drug that is used.⁷⁶

A very large array of synthetic oestrogens and androgens have been examined experimentally, but none appear to offer any clear-cut advantage.

The adrenal steroids, ACTH and Cortisone, have found very wide application in the chemotherapy of the blood cancers, particularly in the

treatment of chronic lymphocytic leukaemia. These hormones have been used either by themselves or often synergistically with 6-mercaptopurine, in the hope that drug resistance would be prevented or at least delayed.

Other anti-tumour drugs

Although the examples of potential anti-tumour drugs already mentioned come from groupings that differ widely in their chemical and biological nature, there are still a few compounds for which claims of clinical utility have been made, which fit into none of these groupings.

Urethane (Fig. 29) is used in the



Fig. 29

treatment of multiple myeloma.⁷⁷ It might owe its activity to anti-metabolic behaviour, but its mechanism of action is not yet known.

Demecolcin (Fig. 30), a synthetic

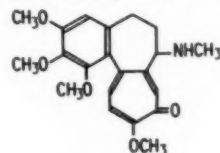


Fig. 30

and less toxic analogue of colchicine, has been considered useful in the treatment of chronic myeloid leukaemia.⁷⁸ Colchicine, a drug derived from the autumn crocus, is well known to biologists for its highly specific anti-mitotic action. It suppresses spindle formation, which is the prior step to the separation of chromosome pairs just before cell division. The effect of this is to prevent cell division and it often leads to the appearance of cells with twice their normal complement of chromosomes.

p-Aminostyrylquinolines (Fig. 31)

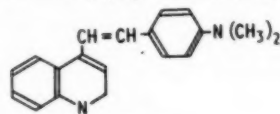


Fig. 31

have been found active against experimental animal tumours, but have not found clinical application.⁷⁹

It would be possible to extend this list with many more organic compounds that have shown activity against experimental animal tumours, but they do not necessarily

add anything to our understanding of the general problem of attempting to control abnormal growth. While the completely empirical approach of literally "trying anything," which is implicit in the massive screening programme under way in America, might produce another "magic bullet," it still seems possible to push forward in a less massive but more rational way. The modification of drugs already known to be growth inhibitors, and the pursuing of anti-metabolites not only of direct nucleic acid synthesis but also of other metabolic pathways, especially those involved in providing the energy for cell metabolism—these seem to be routes along which advance can still be made. The biochemists are all the time attempting to provide more information of the distinctions between normal and malignant growth, and the design of truly successful chemotherapeutic agents may yet have to wait on their fundamental discoveries.

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TWO NEW DRUGS TO COMBAT CANCER

A radio-active drug, developed by a Cambridge University team, has been used in 20 patients suffering from otherwise untreatable malignant tumours of various types. In it is incorporated tritium. The Cambridge team states in the annual report of the British Empire Cancer Campaign that evidence of temporary tumour regression and relief of pain has been obtained in some cases. The report emphasises that no general conclusions can be drawn until further investigation has taken place.

The name of the drug is tritiated tetra-sodium 2-methyl 4-naphtho-hydroquinone diphosphate or tritiated Synkavit. Prof. J. S. Mitchell, leader of the team, acknowledges help from the A.E.R.E., Harwell.

Another new drug described in the report is the steroid Durabolin which has been used on some advanced cases of breast cancer in women. It is stated that "significant and objective improvement" has

been obtained by its use. The experiments with this drug have been taking place in the cancer research department of Westminster Hospital. Forty-seven cases have now been studied, the period of treatment varying from 1 to 18 months. In almost all the cases treated there had been a general improvement in well-being, associated with improved appetite and, in many of the patients, gain in body weight.

The report gives other examples of promising new cancer drugs. One is a Hungarian nitrogen mustard derivative which has now become available in the United Kingdom.

The report draws the conclusion that although a great deal of invaluable research is done with the many individual grants the campaign makes, the surveillance of the vast research fields calls for speciality experts working in teams and that these teams can only be created in the large research centres.

New Drug Testing by Law?

A MOVE was made in the Commons last month (June) to introduce regulations requiring that all new drugs should be tested and evaluated by "a responsible body" before being offered for sale to the public. The proposal was put forward by a Labour M.P.—Mr. George Darling (Hillsborough).

Mr. Derek Walker-Smith, Minister of Health, said that while there were no existing powers under which regulations could be made, he was giving, and would continue to give, all the help and encouragement he could towards improvements in the present arrangements and facilities for clinical trials. He then told the House that the Central and Scottish Health Services Councils, at the suggestion of the Secretary of State for Scotland (Mr. John MacLay) and himself, had agreed to extend the terms of reference and membership of the Standing Joint Committee on the Classification of Proprietary Preparations to enable this Committee to assist.

Copying chemicals

Certain chemicals used in photocopying, such as trichloroethylene and tricresylphosphate, had anaesthetic effects and proved to be drugs of addiction, stated Mr. Barnett Janner (Labour, Leicester, N.W.).

He was concerned at the fact that photocopying work was often carried out by young people in basement rooms, and believed that the problem should be brought to the attention of employers so that they could be warned about it. A Government spokesman with whom he raised the matter said, however, that he was not aware of any problem.

Fertiliser prices

Prices of some products had already been reduced, it was pointed out when complaints were voiced about the high cost of fertilisers during a debate on the Government scheme to extend the subsidy arrangements for another year from July 1.

The report of the Monopolies Commission on Fertilisers was one of the points discussed. Mr. J. B. Godber, Joint Parliamentary Secretary to the Ministry of Agriculture,

Fisheries and Food, was asked why the Government had not acted earlier to deal with prices. He pointed out that having sent the matter to the Commission they had then to await its report. The Government were now having discussions with the industry on the report, he said, adding that many fertilisers would be cheaper in the coming season despite a lowering of the subsidy by about £1,500,000.

"Scurrilous attack"

Mr. Godber defended Lord Netherthorpe (as Sir James Turner he was formerly President of the National Farmers Union) from what he described as "a somewhat scurrilous attack." He was referring to a speech by Mr. Jeremy Thorpe (Liberal, N. Devon) in which he said that it was interesting that the first measure taken by Fisons after being told their prices were too high was to get Lord Netherthorpe and others on to the board. The M.P. added that if the figure of

£151,000 for 1959 was a correct one for directors' fees, he would no doubt "be enjoying some of the benefits of that this year."

In his remarks Mr. Thorpe launched a general attack on the fertiliser industry, saying that the tariff wall protecting it had resulted in high prices, huge profits and vast monopolies. What was needed was a dose of good healthy competition and removal of the tariff, he asserted.

Hazards to animals

A series of experiments with narcotics being carried out by Ministry of Agriculture, Fisheries and Food Officers on a farm near Newmarket was the subject of questions. Mr. G. de Freitas (Labour, Lincoln) asked about the possible danger to animals in the use of crops treated with narcotics for the purpose of killing wood pigeons.

The Minister, Mr. John Hare, said he was aware that there was a danger here, and so far this had been restricted to official experiments.

Correspondence

TO THE EDITOR

DEAR SIR,

pHisoHex and Safer Surgery

Under this title your contributor, A. H. Walters, reviews a paper by Smylie, Webster and Bruce describing the new antibacterial skin cleanser, pHisoHex (February, p. 75). He criticised the methods used by the authors and emphasised that the results of the work by Smylie *et al.* were at variance with the findings of workers in Berlin—Gopel, Rucker and Schutz.

I should like to point out that the findings of both these groups of workers are not at variance, since Smylie *et al.* studied the effect of repeated use of pHisoHex, whereas Gopel *et al.* studied the effects of a single wash; and whereas Smylie *et al.* were able to show near sterility in a good proportion of his cases after repeated use, Gopel *et al.* by his results, if not in his discussion, showed a very marked reduction in bacterial skin counts, which were even further reduced when another count was done at the end of an

operation lasting about 1½-2 hrs., the latter fact indicating that pHisoHex has a cumulative effect.

What is relevant for surgical procedures is the number of bacteria that can be liberated from the skin through the glove of the operator. Smylie *et al.* has given part of this answer and his work has been elaborated by recent findings of Lowbury and Lilly, who showed when comparing pHisoHex with other methods of pre-operative skin preparation that pHisoHex was the most efficient of these agents in reducing the number of bacteria which appeared through small punctures in surgical gloves of persons carrying out mock operations.

These findings, and those of the other papers mentioned by me above and discussed by A. H. Walters, demonstrate the effectiveness of pHisoHex, which in the past has been shown in large numbers of comparative clinical series.

K. BOHEIMER, M.B., B.S.

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Kingston-on-Thames.

Recent Trends in Evaporator Design

By P. J. King,* B.Sc., Ph.D.

The evaporators discussed in this review are those for handling comparatively valuable and/or heat-sensitive materials in the pharmaceutical and fine chemicals industry. Dr. King surveys the important trends in research and design published since our last review of evaporators, which appeared in June 1957. He includes a short section on the selection of equipment, design and economics.

DESIGN TRENDS

AN ARTICLE on the design of evaporators for the fine chemicals industry was presented in this journal in June 1957,¹ and the present review describes the more interesting and important developments in research and design published since that date. As in the previous review, the field of reference has been restricted to evaporators of particular interest in the fine chemicals industry. In general this has been taken to mean evaporators to handle comparatively valuable and/or heat-sensitive materials. Less attention has been paid to heat (steam) economy, improved efficiency and scale formation than to the four requirements listed below.

- Low absolute temperature of the liquor.
- Low temperature difference between the heating medium and the liquor.
- Short time of residence.
- Minimum loss by entrainment.

The main headings under which the work will be discussed are:

- Research.
- New and improved design.
- Selection of equipment, design and economics.

Research

Published work in this field during the past few years has been almost entirely concerned with the climbing film evaporator. This apparatus is well known to the chemical industry, having first appeared commercially in the early years of this century. However, since the war much effort has been expended on research designed to extend the usefulness of the apparatus, especially to heat-sensitive materials, and to lead to an understanding of the fundamentals of its operation. Descriptions of commercial apparatus using this principle will be found in most unit

operations textbooks, e.g. reference 2.

In 1956 Whitt³ studied the performance of three sizes of climbing film evaporators, evaporating organic liquids with Prandtl Nos. of between 2 and 3 and with viscosities of about 0.3 centipoise. Hot-water heating was used and the evaporator tubes were made of silver. A constant L/D ratio was employed, with tube sizes $\frac{1}{8}$ in. by 5.17 ft., $\frac{3}{8}$ in. by 7.5 ft., and 2 in. by 20 ft. Temperature difference was in the range 8.5-41.5°C.

Under these conditions there was little effect of solution concentration on the rate of evaporation, and almost complete evaporation was obtained for all dilutions used. However, there was evidence for the existence of a critical temperature difference between the heating medium and the vaporising liquid.

NOMENCLATURE

A	area.
C	sp. heat.
D	tube diameter.
g	accel. due to gravity.
G	mass flow rate.
h	height of evaporation area.
h_b	boiling film coefficient of heat transfer.
J	conversion factor (718 ft. lb. = 1 B.T.U.).
k	thermal conductivity.
K	a constant ($\frac{1}{3}$ if D is in ft.).
K_o	a constant.
L	tube length.
n	an exponent.
N	rpm of motor.
ρ	a constant.
P	power requirements.
Q	heat flux.
r_1	radius of rotor blades.
r_o	radius of rotor shaft.
R	resistance to heat transfer.
t_2	clearance between rotor blade tip and tube wall.
U	overall coefficient of heat transfer.
w_f	mass flow of feed.
x_o	concentration of solution at tube entry.
Δt	temperature difference.
Δt_b	boiling film temperature difference.
λ	latent heat.
μ	viscosity.
ρ_L	density of liquid.
σ	surface tension.
ω	rotor angular velocity.
φ	some function.

This resulted in a falling-off of the overall heat transfer coefficient (U) in a maximum value of heat flux of about 12,000 B.T.U./(sq. ft.)(hr.) and with a critical film temperature difference of about 20°F. Up to this value of critical temperature difference, the heat flux (Q) increased with temperature difference (Δt) and could be represented by:

$$Q/A = 100 \Delta t^{1.25} \text{ B.T.U.}/(\text{sq. ft.})(\text{hr.}) \quad (1)$$

(Δt in °F.)

On the basis of the experiments it was concluded that the design methods proposed by Kern⁴ for natural circulation evaporators could be applied to the design of climbing film evaporators. Later the same year Lee, Dorsey, Moore and Mayfield⁵ published additional information for natural circulation (thermosiphon) evaporators obtained for a variety of liquids at various pressures, the data being successfully correlated. The liquids investigated included water, acetone, propylene glycol, n-propanol, ethyl toluene, benzene and n-butane, and pressures ranged from 0.1 atm. to 10 atm.

Cathro and Tait⁶ in 1957 made a detailed investigation of the boiling action inside a climbing film evaporator. They investigated eight liquids boiling inside four different tubes and they correlated their experimental data, together with much of the published data by equation 2. This equation was obtained by the process of dimensional analysis

$$\left(\frac{DG}{\mu}\right)^{0.25} \left(\frac{D \rho_L \lambda J}{\sigma}\right)^{0.48} \left(\frac{L}{D}\right)^{0.7} \left(\frac{D}{K}\right)^{0.5} = \varphi \left(\frac{\Delta t_b C}{\lambda}\right) \quad (2)$$

In the experimental work reported in the paper the following variations in the various dimensionless groups were made:

$(\Delta t_b C/\lambda)$	30 : 1	$(D \rho_L \lambda J/\sigma)$	3 : 1
$(h_b D k)$	30 : 1	(L/D)	2 : 1
(DG/μ)	25 : 1	(D/K)	2 : 1

Most of the above groupings are readily recognisable, the group

* Department of Chemical Engineering, Fuel Technology and Metallurgy, The Manchester College of Science and Technology.

$(\Delta t_b C/\lambda)$ is significant in problems concerned both with condensation of vapour and with film boiling, it expresses the ratio of the superheat in the liquid film to the total heat transferred. The group $(D_p \lambda / \sigma)$ is the ratio of the mechanical and the thermal energy required to produce new surface.

The exponent of 0.25 on the $N_{Re}(DG/\mu)$ in equation (2) was only applicable above a certain critical value, but with this limitation the equation correlated available data to within $\pm 30\%$. However, it was reported to be only applicable to pure liquids or perhaps to small degrees of concentration. With more concentration it was suggested that equation 3 should be used. This equation was developed by taking mass and enthalpy balances over a differential section of the column and integrating the result.

$$Q + (\lambda p W_f x_0) \left[\ln \frac{W_f(1 - p x_0)}{W_f(1 - p x_0) - (Q/\lambda)} \right] = K_o A \Delta t_b^{0.25} \quad (3)$$

Dengler and Addoms⁷ studied the heat transfer mechanism for the vaporisation of water in a 20 ft. by 1 in. vertical copper tube. They concluded that (1) the mechanism was primarily convective. Nucleate boiling was dominant only under conditions of low liquid velocity and was gradually depressed by the effects of vapour velocity which induced forced convection. (2) The operating variables exerted an independent and often contradictory effect on each of these mechanisms, for example:

- Increase of pressure may have increased the heat transfer coefficient, because it increased nucleate boiling, or it may have decreased the coefficient, in the range of two-phase convection, by having raised the average gas density and hence lowered the velocity.
- Increase in temperature difference promoted nucleate boiling, but had no direct effect on convectional coefficients.
- Increase in total mass throughput increased the convectional heat transfer, but decreased nucleate boiling heat transfer by lowering the available effective temperature driving force for nucleation.

In 1958 Pepper⁸ made a fairly complete assessment of available published data on climbing film

evaporators and analysed the factors which should be important for the design of equipment. The general conclusion arrived at was that it was possible to design climbing film evaporators from available data for aqueous or similar solutions if tube diameters were less than 1 in., but for larger tubes or for different liquids it was necessary to extrapolate data (some of the difficulties could be overcome by redesign in order to use a multiple of smaller tubes).

On the basis of this assessment, evaporators had been designed for the A.E.R.E. and were reported to have come up to design performance. An example was given of a $1\frac{1}{8}$ in. 8 ft. nickel tube heated by steam. The design was to handle 750 ml./min. of dilute sodium hydroxide solution to give 375 ml./min. of concentrate. The designed value for the overall heat transfer coefficient was 548 B.T.U./sq. ft. (hr.) (°F.) and the actual value was found to be 516 B.T.U./sq. ft. (hr.) (°F.).

Also in 1958, Doll-Steinberg⁹ published the results of an investigation into the performance of two monel metal tubes 95 cm. long (one 1.13 cm. i.d., 1.17 cm. o.d.; the other 0.735 cm. i.d., 0.77 cm. o.d.). The investigation covered such factors as the effect of liquid submergence and temperature difference on the water circulation rate and on the heat transfer coefficient. The results were expressed graphically; in general it was found that below a certain value of temperature difference, which was greater at higher submergences, the heat transfer coefficient varied as $\Delta t^{0.3}$ (Δt in °C.). There followed a region where the exponent on the temperature difference became greater, the actual value (which was reported to vary between 0.6 and 0.95) depended both on submergence and on tube diameter. Finally, at higher values of Δt , a falling-off of the coefficient was reported. This maximum value is in line with other workers who have reported the existence of a critical temperature difference.³ A qualitative explanation of these results was made in terms of the superheating of, and bubble formation in, the boundary layer.

Similar results were reported for the effect of Δt on the liquid circulation rate. In this case four regions were reported. As Δt increased from a low value, there was a rapid rise in circulation to a maximum value, where it remained almost constant.

(At high submergences in the large tube this maximum value extended over a wide range of Δt , but at low submergences in the small tube the maximum value only extended over a small range of Δt .) The rate then fell off almost linearly with intermediate values of Δt and finally attained an almost constant or slightly decreasing rate at high values of Δt . These results were also explained qualitatively, in this case in terms of "slip" between the vapour and liquid.

Recent Soviet research has been reported by Jackson,¹⁰ who states that Tobilevich and Shchegolev¹¹ investigated the overall resistance to heat transfer in a climbing film evaporator and divided the overall resistance into the usual individual resistances (equation 4).

$$R = R_1 + R_w + R_d + R_s \quad (4)$$

R_1 is the resistance for the condensing steam.

R_w is the resistance of the tube wall.

R_d is the resistance of the dirt layer.

R_s is the resistance of the boiling liquid.

The data for a number of evaporators (for which no details were given) were reported to show the relationship expressed in Table 1.

Table 1.¹⁰ Relationship between individual and overall resistances for various effects

Resistance	Proportion of overall resistance (%)			
	1st effect	2nd effect	3rd effect	4th effect
R_1	20	10	6	4
R_w	5	4	3	1
R_d	30	36	31	25
R_s	45	50	60	70

Hence it would appear that the most useful reductions would be to resistances R_d and R_s . Fig. 1 shows the variation in heat transfer coefficient with tube height. In general, there were portions of the tube (the boiling section) where heat transfer rate was high, and other portions where it was very low (the heating section at the base and the upper part of the tube where there was much vapour). The proportion of the tube length occupied by each section was found to depend on circulation velocity. For example, at low circulation rates the heating section was small, but the section containing boiling liquid with a high vapour content was large and above this there was a section containing virtually wet steam, hence the overall coefficient of heat transfer was small. As circulation rate rose, the section containing a high proportion of vapour decreased, but the preheating section became larger.

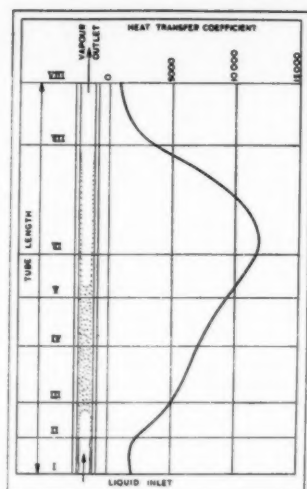


FIG 1

Variation in heat-transfer coefficient (kcal/m² hr. °C.) over the tube length. (1) Heating section. (2) Boiling section. (3) Emulsion section. (4) Plug flow section. (5) and (6) Annular flow section. (7) Wet steam. (8) Saturated steam.

(Source J. Jackson, *Brit. Chem. Eng.*, 1960, 5, 271 (Fig. 2).)

New and improved design

The data reported in Table I show that the greatest resistance to heat transfer for liquid boiling inside tubes lies in the liquid film; it is not surprising therefore that a number of evaporators proposed or modified during the past few years have incorporated devices designed to reduce this resistance. The general solution^{12,13,14,15} has been to place a rotor inside the evaporator tube and to attach wipers to this rotor. This device has been applied to both falling and climbing film evaporators. Without mechanical aid the film (particularly the falling film) tends to be unstable and dry spots develop on the heated tube wall. To avoid this and also to provide agitation of the liquid film, wipers or blades are attached to a rotor arranged concentrically inside the tube. These wipers may either be arranged to just clear the tube wall, to give a fixed film thickness of 1-2 mm. as in Fig. 2a, or may be hinged so as to press on the tube wall by centrifugal force (possibly supported by the addition of springs) as in Figs. 2b and 5. In this case the film thickness is controlled by a balance between the pressure exerted by the blades and the resistance caused by the viscosity of the liquid.

In 1957 Gudheim and Donovan¹⁵ described three types of evaporator (Fig. 3) which utilised the agitated thin film principle of heat transfer. In each of these, rotating blades turned inside a cylinder or truncated cone, developed a centrifugal force in the process liquor, and caused a violently agitated film to form on the circular wall. The hold-up was reported to be small, and by suitable control of feed rate, etc., residence time could be reduced to a few seconds. The effect of feed rate variations and the use of vacuum was discussed and Table II shows some of the data reported for overall heat-transfer coefficient. It was claimed that this type of evaporator would give liquid side coefficients of the same order as for the steam side.

Table II.¹⁵ Values of overall resistance reported by Gudheim and Donovan.

Substance	Overall heat transfer coefficient U [(B.T.U.)/(sq. ft.) (hr.) (°F.)]
Acetic acid	745
Fatty acids	330
Isopropyl alcohol ..	400
Methyl alcohol ..	650
Water	700

A detailed investigation of this type of unit was made in 1959 by Lustenader, Richter and Neugebauer.¹⁶ The evaporator used was a vapour compression unit, where the evaporated liquid (water vapour) was compressed and used to provide heat for further evaporation. The apparatus consisted of a copper tube 24 in. long and 3 in. diameter with a wall thickness of 0.035 in. The outer annulus (heating jacket) was provided with transparent walls so that the condensation of the heating vapour could be studied. The investigation was carried out with low values of temperature difference and it was assumed that under these conditions there would be no bubble

formation. Three conditions were postulated as shown in Fig. 4.

- Condition (a) would occur at low wiper speeds, when dry spots would be formed before the wiper could redistribute the film. In this case only a portion of the surface would be utilised.
- (b) would occur with increase in rotor speed and represents the state at which all the surface was just wetted all the time.
- (c) at higher speeds there was an increase in average film thickness. (The limit is an infinite speed for the wiper and a constant film thickness.)

Each case was analysed and it was shown that the maximum heat was transferred under condition (b). It was also reported that the temperature difference and the wiper speed had no influence on the magnitude of the maximum or minimum value of the overall heat transfer coefficient; this was determined by the initial film thickness and the condensing side heat-transfer coefficient. In an investigation into the importance of the condensing side coefficient it was shown that a grooved or fluted surface gave a much higher value of heat transfer than a smooth polished surface. They obtained a maximum value of overall transfer coefficient of 8,300 B.T.U./(sq. ft.) (hr.) (°F.) and the tests indicated that the fluted surface had an average condensing coefficient of approximately 10,000 B.T.U./(sq. ft.) (hr.) (°F.), at an overall Δt of 1.5°F. (this is approx. four times larger than would be expected for a smooth surface of the same dimensions). They used several different types of wiper design, but the final version is shown in Fig. 5. The brushes are of

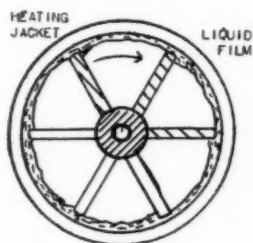
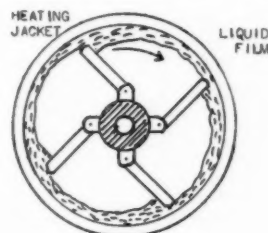


FIG 2 a



2b

**Agitated thin film evaporators
(a) Fixed blade. (b) Hinged blade.**

(Source R. Schneider, *Chem. Ing. Tech.*, 1955, 27, 257-61.)

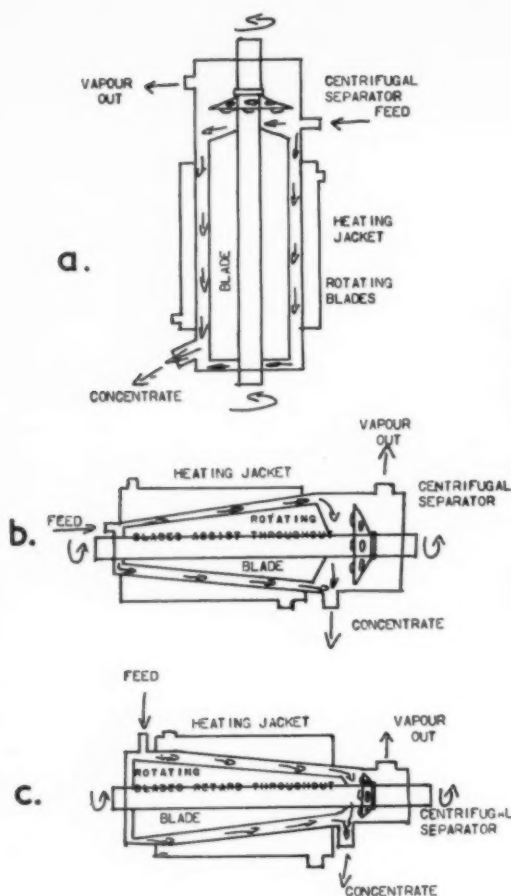


FIG. 3

carbon with bronze screening as the back up springs.

Hadley and Thomas¹⁷ recently published a mathematical and experimental study of the agitated thin film evaporator. The experimental apparatus closely resembled that described by Haley.¹³ An equation (5) was developed for the critical angular velocity (ω_0) below which a portion of the evaporator tube became filled with liquid.

$$\omega_0 = \sqrt{\frac{2gh}{(r_1^2 - r_0^2)}} \quad (5)$$

Equations were developed and confirmed experimentally for the volume hold-up with angular velocities both above and below the critical. The power requirement (in h.p.) for this type of evaporator was given by equation 6.

$$P = 0.263 \times 10^{-8} \left(\frac{hr_1^3}{r_2} \right) N^2 \mu \quad (6)$$

It was observed that any design of

this type must be a compromise between high volume hold-up and residence time, and high power requirements, because with increase in rotor speed the power requirements increase rapidly and it is not satisfactory to operate at low speed because of a low value of heat transfer coefficient. Also since volume hold-up was found to be virtually independent of radius, whilst power requirements varied as radius cubed, it was concluded that a minimum radius and a maximum height should be employed with columns of this type.

Other developments

The use of submerged combustion in evaporators was discussed by Cronan¹⁸ in 1956, and particular mention was made of the use of this technique for the concentration of whey—a heat-sensitive material. The use of hot combustion gases for the evaporation of heat-sensitive mater-

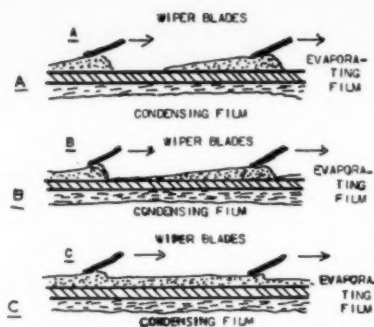


FIG. 4

Film flow in agitated evaporators¹⁸

- (a) Low wiper speed.
- (b) Intermediate wiper speed.
- (c) High wiper speed.

(Source Lustenader et al., A.S.M.E. Trans. 1959, 81(c), 297-307.)

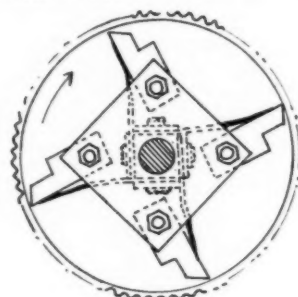


FIG. 5

Sketch of a spring loaded carbon wiper assembly¹⁸

(Source as for Fig. 4.)

ial by direct contact was the subject of a recent patent,¹⁹ a sketch to illustrate the principle of this design is shown in Fig. 6. There was an inner chamber (A) full of a non-charrable, condensable fluid (usually water), this chamber was positioned below the level of the liquid in the evaporator shell. (B) The hot combustion gases passed into this inner chamber and bubbled through the water. During their passage through the water the gases cooled and some of the water was evaporated. The mixture of gas and vapour was then passed through a coil (C) also submerged below the surface of the heat-sensitive material. In this coil most of the water vapour condensed—the latent heat of condensation being passed through the tube wall into the liquid. The non-condensed gas was separated from the water in a gas-liquid separator (D), the liquid water being pumped back into the

inner chamber. All or part of the now cooled gas was passed into the shell of the evaporator and its remaining heat was given up to the heat-sensitive liquid by direct contact. The usual condensing equipment etc., was attached to the outlet (E) of the evaporator shell.

A further type of evaporator for heat-sensitive materials has recently been described.²⁰ A sketch is shown in Fig. 7. The design utilised a circulating stream of inert gas. Liquid was pumped into this stream at point A. The mixture was heated and a portion of the liquid evaporated in order to partially saturate the gas. The non-evaporated liquid was separated at B and the vapour-gas mixture cooled by heat exchange with the liquid-gas stream and finally cooled and separated at C. The inert gas, which was virtually free of vapour, was recirculated by a pump. Provision can be made for this design to operate in two or more effects.

SELECTION OF EQUIPMENT, DESIGN AND ECONOMICS

Selection of equipment

Many types of evaporator are commercially available and the choice of the optimum for any particular case is difficult. The solution to this problem lies in the integration of solution characteristics, evaporator type characteristics and the economics of capital equipment and operating costs. A few of the variables which have to be considered are the physical properties of the solution to be evaporated, maintenance costs, labour costs, cooling water costs and equipment characteristics—such as hold-up, throughput, residence time, etc.

An examination of some of these variables together with suggested solutions for a few illustrative cases was made by Coston and Lindsey²¹ in 1956. A few of the suggestions may be summarised.

Liquid viscosity

Up to 100 cps.: a long tube vertical or a calandria type, forced circulation may be useful.

6-100 cps.: forced circulation, agitated thin film or falling film.

Above 100 cps.: drying equipment must be used or slow evaporation from an agitated film evaporator.

Heat-sensitive materials low temperature (high vacuum). Use forced circulation or falling film types. The agitated thin film is particularly useful because of

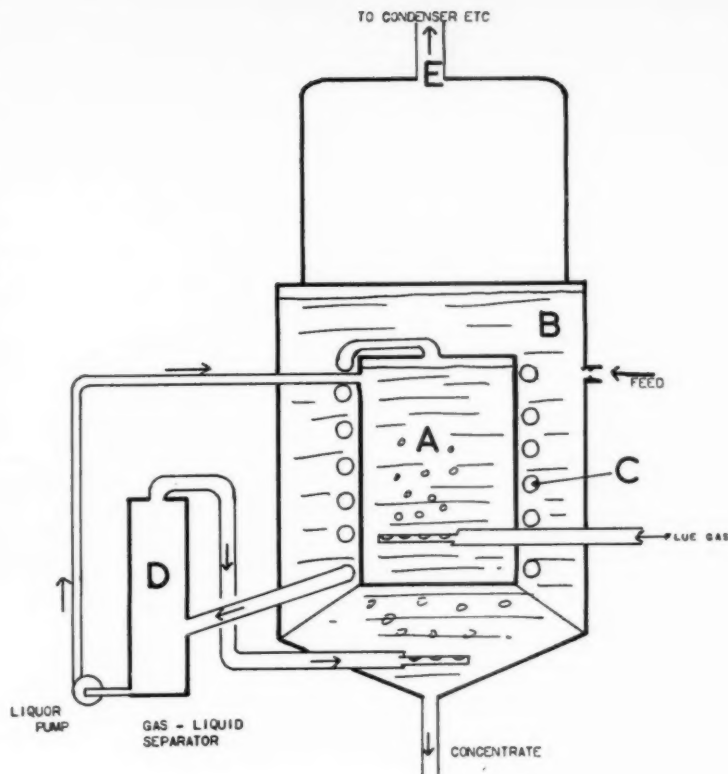


FIG. 6

An evaporator using direct flue gas heating for heat sensitive materials

(Source U.S. Patent 2,834,409.)

the short time at temperature characteristics.

An example quoted by Coston and Lindsey for the concentration of orange juice suggested the use of

either a falling film with recirculation of the liquor or an agitated film evaporator.

Coates and Pressburg²² recently published a simplified method for

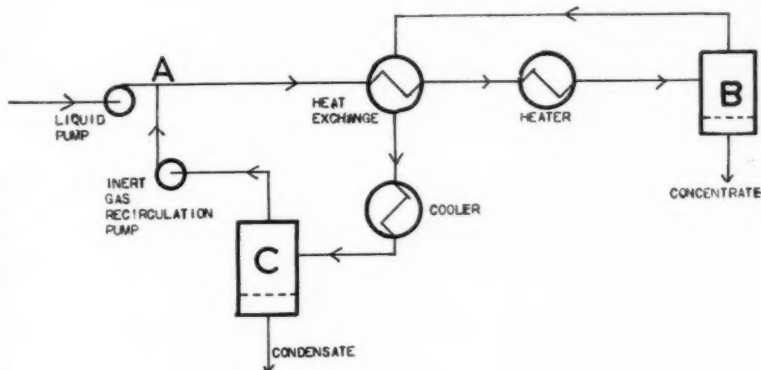


FIG. 7

An evaporator using a recirculating inert gas stream

(Source Brit. Patent 822,810.)

the solution of multi-effect evaporator problems. This method, which is less time consuming, is claimed to check on the average to within 2% of the more exact calculation and a maximum error of 7% is reported.

Cost factors

The importance of physical design, flow sheet and heat reclamation in the design and costing of evaporators was illustrated by Kohlins and Englander²³ in 1956. An attempt was made to show how savings could be effected.

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ALDERLEY PARK

(Continued from page 283)

opened—has now been reduced to about 25, indicating greater concentration on fewer objectives. Of course, even with research on the Alderley Park scale we cannot expect miracles. It puts the gigantic problem of chemotherapy into perspective to recall that in the United States one group of diseases alone—the cancers—inspires the screening of no fewer than 40,000 compounds a year. The research director at Alderley Park, Dr. W. A. Sexton, and his three colleagues—Dr. D. G. Davey (biology), Dr. F. L. Rose (chemistry and biochemistry) and Dr. H. C. Carrington (administration), are perpetually faced with the task of distinguishing the possible from the desirable, of assessing resources and objectives and deciding on which sections of the enormous front they should deploy their limited forces. They do not expect miracles but hope for a fair share of good luck.

Industry's Publications

Light fittings. Benjamin Electric Ltd. have issued an attractive folder describing and illustrating their new range of *Litemaster* fluorescent lighting fittings (see *MANUFACTURING CHEMIST*, May, p. 214).

Paper history. Samuel Jones and Co. Ltd. have issued a handsome booklet called "150 Years on Paper" which describes the past, present and future of the company. Interleaved are pages listing important historical dates since the company was founded 150 years ago. The firm's range of papers and packaging products are described and illustrated.

Sturtevant products. A new catalogue of the extensive range of machines made by Sturtevant Engineering Co. Ltd. has been issued. It runs to 59 pages, is well illustrated and strongly bound.

News and Review. Gallenkamp-Towers, the new laboratory furnishing organisation formed by the acquisition of J. W. Towers and Co. Ltd., by A. Gallenkamp and Co. Ltd., have started a biannual publication with this title. The first number contains company and personal news, information on various

instruments and apparatus, and details of sales and service arrangements. Particulars of new quantity discounts are also given.

Hydroquinone. May and Baker have issued a handy guide to the industrial uses of M hydroquinone and its derivatives.

Industries, products and government departments. In connection with the revised "Directory of Board of Trade Departments and their Work," published with the *Board of Trade Journal*, a new alphabetical "Index of Industries and Products with the Government Departments Principally Concerned" has been published separately in order to assist enquirers who require a detailed index covering the Board of Trade and other Ministries. This index is obtainable on request from the Librarian, Board of Trade Library, Horse Guards Avenue, S.W.1, priced at 2s., including postage. Money should be enclosed with order.

Monsanto Hianqpyi Huahshyue Piin, well known in the Western world as Monsanto rubber chemicals, will become more familiar throughout the Orient now a

technical bulletin on rubber chemicals printed in Chinese has been produced by Monsanto Chemicals Ltd. It is believed to be the first of its type produced by any British chemical manufacturer. The booklet was designed and printed in Singapore, and care has been taken to ensure an idiom acceptable in Singapore, Hong Kong, Formosa and South Korea.

Edinburgh Occasion. Under this title Duncan Flockhart have issued an account of the sixth Lister memorial lecture given on October 1, 1959, by Dr. Nathan Eddy, the subject being "Chemical structure and action of morphine-like analgesics and related substances."

Sequestering agents. A data sheet has been issued by Robinson Bros. Ltd. on 1,4-di(carboxymethylthio)butane and 2,2'-di(carboxymethylthio)diethyl ether. These materials are available in experimental quantities. Their suggested use is as metal deactivators or sequestering agents in those cases where ethylene diamine tetra-acetic acid (E.D.T.A.) or its homologues are ineffective, especially in acid or non-aqueous media.

Chemistry and Colour Photography

THE organic chemistry of colour photography was the title of a lecture given recently to the Fine Chemicals Group of the Society of Chemical Industry in London. The chairman of the Group, Dr. J. D. Kendall (Ilford Ltd.), introduced the lecturer, Dr. E. B. Knott.

Organic chemicals have been used for the manufacture and processing of photographic materials since the development of the art in 1840. These chemicals, including black-and-white developing agents, colloids such as gelatin, its replacements and derivatives, sensitising dyes, sulphur sensitisers, emulsion stabilisers, development accelerators, super-sensitisers, surface-active coating aids, etc., are mainly essential components of both black-and-white and colour photographic systems without contributing towards the actual chemical formation of the coloured image. The latter reaction, the addition of oxidised colour developer to the colour coupler to give the leuco-dye, and the oxidation of the latter to the dye itself, is essentially the only reaction not common to both systems.

The reason for the use of yellow, magenta and blue-green dyes in popular colour material for reproducing any coloured object was explained by reference to Maxwell's experiments in additive colour reproduction and to the relationship between the additive and subtractive colour theory.

In order to obtain separate records of the blue, green and red light reflected from a subject, three layers are coated successively on to a support, each of which is sensitive to one of these three colours. The requirements of the sensitising dyes used to confer green and red sensitivity on two of these layers were given.

An imagewise formation of a dye of the correct colour in each layer is achieved by selective development or by incorporated coupler development. Both methods depend on the formation of oxidised developer in those areas where the exposed silver halide is reduced to silver, and its coupling with an organic compound present during its formation. Selective development, suitable only for reversal processes, uses three successive colour developers, each layer being developed to its correct colour in turn, the coupler being present

in the developer. On the other hand, when the coupler is incorporated in its correct layer before coating, a single colour development produces all three dyes in one step. The steps involved in selective and incorporated coupler reversal processing and in incorporated coupler negative-positive processing were described.

Developers and couplers

The properties and structural requirements of NN-disubstituted *p*-phenylenediamine colour developers and of colour couplers were reviewed. The latter all contain an acid hydrogen atom and a nucleophilic centre. They are typified by substituted phenols and naphthols which yield blue to blue-green dyes and by open-chain and cyclic ketomethylene compounds yielding yellow or magenta dyes. The most popular yellow couplers are derivatives of benzoylacetyl, the most popular magentas being 1,3-disubstituted 5-pyrazolones. Sufficient is now known about the relationship of colour and structure to enable one to tailor the molecules to give dyes with desirable light absorption characteristics.

In its simplest form, the formation of dye occurs by the replacement of a hydrogen atom of the coupler molecule by the developer molecule. Elimination-coupling reactions can, however, also occur by the elimination of an atom or group other than hydrogen. Examples of such reactions are provided by coloured couplers used in correcting for the unwanted absorption of the cyan and magenta dyes.

The mechanism of dye formation in coupling development was described and some aspects of dye-image stability were discussed.

Discussion

At the end of Dr. Knott's lecture the following questions were asked:

Q. Mr. J. Blair asked:

Can Dr. Knott confirm my impression that colour negatives possess a much finer grain than black-and-white negatives, as I find that very much better black-and-white enlargements result from colour negatives?

A. Dr. Knott replied:

In the printing of colour negatives on to bromide paper it is

mainly the yellow layer which functions as the negative, since the bromide paper is only sensitive to variations in intensity of blue light. Because of the thinness of this layer a sharp print results. On the other hand, it is usual for a print from a colour negative to be at least as grainy as a print from a black-and-white negative of similar grain size.

Q. Mr. J. H. Hunt asked:

In a three layer emulsion there is presumably generalised absorption of light by the silver halide. Does this require that the lower layers be relatively more sensitive to their respective colours to compensate for the reduced intensity of the light reaching them?

A. Dr. Knott replied:

Yes, the sensitivities of the lower layers are higher than that of the top, blue-sensitive layer since, although the latter does not absorb an appreciable amount of green or red light, some loss of intensity results from light scatter by the top layer.

A vote of thanks was proposed by the vice-chairman, Dr. A. C. Newman, and carried with acclamation.

TWO-PART DENTIFRICE

A two-part dentifrice in which the individual compositions may be used independently or together is the subject of a recent Belgian patent (562,960). Prepared separately so as to avoid interaction between the materials prior to use, exceptional cleaning and tooth brightening action is claimed for the formulation, which is compounded as follows:

I		g.
Glycerol	2,000
Magnesium carbonate	800
Tricalcium phosphate	150
Kaolin	50
Gum tragacanth	85
Foaming agent (alkylsulphate)	60
"Solparol"	2-5
Water	1,850
		blended to make a paste
II		
Tricalcium phosphate	20
Sodium bicarbonate	110
Magnesium carbonate	20
		blended to make a powder

Analytical Chemistry

By W. I. Stephen, PH.D., A.R.I.C.

*Herbicides and pesticides • Detergents • Pharmaceuticals • Vitamins
Antibiotics • Drugs • Fine chemicals*

ONE of the most rapidly expanding branches of applied chemistry is agricultural chemistry with its development of economically important chemicals for use as fertilisers, as insecticides and other pesticides, or as herbicides. This last group of chemicals, which includes the selective weedkillers, has a vital rôle to play in increasing world food production, and considerable amounts of these substances are now being manufactured. From the analytical standpoint, there are few major problems connected with the analysis of the bulk materials, but their extreme sensitivity to certain forms of plant life makes the development of analytical methods for trace amounts of these chemicals an important task for the analyst. Unfortunately, few methods have been reported for this type of analysis, but this month's report begins with an account of recently published methods of general analytical interest.

Herbicides

In the previous report in this series,¹ mention was made of the analysis of phenoxymethylpenicillin which included a colorimetric determination of phenoxyacetic acid based on a nitration and extraction procedure. As little as 5 µg. of phenoxyacetic acid can be determined by this means. Such procedures could probably be applied to the halogenated phenoxyacetic acids. Bark and Graham,² in a study of the additive effect of substituent groupings in chromatographic separations, have examined a number of economically important members of this class of compound, and although their work was not directed specifically to obtaining analytical

methods for these substances, there are obvious applications for their procedures. Hungarian workers³ have studied the u.v. absorption of ethereal solutions of T.C.A. (trichloroacetic acid), 2:4-D (2:4-dichlorophenoxyacetic acid), 2:4:5-T (2:4:5-trichlorophenoxyacetic acid) and 4-chloro-2-methylphenoxyacetic acid over the wavelengths 210-350 mµ. A linear relationship exists between the concentration of these acids (1-10 mg. per 100 ml.) and the extinction at maximum absorption which can be used for quantitative purposes. Any of the three phenoxyacetic acids can be determined in the presence of T.C.A. Further studies⁴ on these compounds indicate that T.C.A. can be determined polarographically in the presence of 2:4-D without incurring any error, and a new polarographic procedure using tetramethylammonium iodide as supporting electrolyte has been developed for the determinations of the three phenoxyacetic acids. Haddock and Phillips⁵ have developed a method for the determination of α(4-chloro-2-methylphenoxy) propionic acid in the commercial product. A chromatographic separation on Hyflo Super-Cel is used to isolate this acid from such impurities as the 4:6-dichloro acid, the 6-chloro acid and the 2-methyl acid. The elution procedure gives three main fractions, the second of which is shown to contain the 4-chloro-2-methyl acid. The extinction of this eluate is determined at 287 mµ and the concentration of acid is obtained from a reference curve. β-Phenoxypropionic acids do not interfere because they are eluted before the α-acids. The method has proved satisfactory for material containing at least 75% of the active constituent.

Infra-red data are given for the analysis of mixtures of the butoxyethoxypropyl esters of 2:4-D and 2:4:5-T and for the isopropyl and butyl esters of 2:4-D and 2:4:5-T.⁷

Pesticides

Fischer⁸ has described a paper-chromatographic technique for the identification of antu [1-(1-naphthyl)-2-thiourea] after extraction into acidified ether. A methanolic solution of the residue after evaporation of the ether is first made and this solution is spotted on to S. and S. paper No. 2043, and subjected to ascending chromatography with the solvent system, ethanol, amyl alcohol, aqueous ammonia in ratios of 2:2:1. The dried paper is sprayed with a hypobromite solution which shows up the antu as a violet spot at R_f 0.79. About 30 µg. is the minimum amount detectable. Armstrong⁹ has made recommendations for the determination of warfarin in rodenticides. For warfarin concentrates (0.5%) the standard Ministry of Agriculture procedure can be used. This involves extraction of the sample at room temperature with isopropanol containing 1% (v/v) of acetic acid. The clear extract is examined spectrophotometrically at 271, 282 and at 305.5 mµ using a similar extract of pure oat flour as a blank. The extinction of the extract at 305.5 gives the amount of warfarin present. Concentrates based on maize flour or china clay need no blank determination.

A new colour reaction for dieldrin and endrin¹⁰ involves their isomerisation to the 6-oxo derivatives by heating with boron trifluoride in diethyl ether. The 2:4-dinitrophenylhydrazones of these ketones give a red colour on treatment with tetraethylammonium hydroxide which can be used to detect 10 µg. of the insecticides. The presence of 1 mg. of DDT or BHC has no detrimental effect. Strache¹¹ determines BHC and DDT in commercial preparations by a combination of two procedures. The sample is first saponified with ethanolamine to yield three equivalents of chloride ion per mole of BHC and one equivalent of chloride ion per mole of DDT. Reduction with sodium and 2-propanol on a fresh sample releases

the five chlorine atoms in DDT and the six in BHC. Two Volhard titrations enable the proportions of each substance in the sample to be determined. Procedures for the detection of BHC have been described by Rathenasinkam.¹²

The microdetermination of TDE [Perthane, 1:1-dichloro-2:2-di-(*p*-chlorophenyl)ethane] is effected, after extraction from plant material by reacting it with sodium methoxide in dimethylformamide.¹³ This gives 1-chloro-2:2-di-(*p*-chlorophenyl)ethylene which on treatment with sulphuric acid gives a coloured carbonium ion having an absorption maximum at 502 m μ . About 1.0 μ g. of TDE can be detected. Roth¹⁴ has made a study of the colorimetric determination of TDE and mixed TDE-DDT residues. Like DDT and related compounds, TDE can be nitrated and the product can be extracted into benzene; unlike DDT and related compounds it does not then react with sodium methoxide to give a coloured product. Colour can, however, be developed by refluxing the nitrated material with N-ethanolic potash and then acidifying. This colour can be used as a basis for the selective colorimetric determination of TDE.

Detergents

Russell and Whittaker¹⁵ have found the equivalent weights of a number of wetting agents by an ion exchange method. *Zeokarb* 225 is converted to its hydrogen form in the usual way and a warm solution of 0.5 g. of the wetting agent in 50 ml. of water is passed through the resin bed. The column is washed with warm water until 200 ml. of eluate have been collected, and this is titrated with 0.1 N-sodium hydroxide to the methyl red end-point. A blank determination is necessary. Both anionic and cationic wetting agents give results which compare favourably with those of other methods. *Teepol* 530 gives high results because of the presence of potassium salts. An ion exchange method is also recommended for the analysis and purification of mixed anionic and non-ionic detergents.¹⁶ The anionic material is adsorbed on an ion exchange resin after removal of cations on a strongly acid resin; the non-ionic material passes through the resin bed and is recovered in the percolate. The anionic material is eluted from the column with a caustic soda solution (2% in 50% aqueous *iso*-propyl

alcohol) and is then isolated as the sodium salt. Mixed bed techniques can also be used. Slack¹⁷ has simplified the procedure of Longwell and Maniece¹⁸ for the determination of anionic detergents in sewage effluents and river waters. The main advantage is the considerable saving in time by the use of the new method.

Schaller¹⁹ has described suitable tests for establishing the purity of sodium lauryl sulphate and a method for the assay of this substance, based on an earlier method due to Wickbold. The precipitation of this substance with *p*-toluidine in aqueous solution is quantitative and the precipitate is extracted into ether and titrated with an ethanolic solution of sodium hydroxide to the cresol red end-point. As little as 0.2 g. can be determined with an error of +0.2%. Recoveries of specially purified material are about 99.86%; the average equivalent weight is 305.5. A subsequent paper by the same author²⁰ details the application of the *p*-toluidine procedure to the determination of sodium lauryl sulphate in ointments.

Holness and Stone²¹ have published an addendum to their systematic scheme of semi-micro qualitative analysis for anionic surface-active agents.²² A new test is described which is integrated with the general scheme of analysis.

Pharmaceuticals

Automatic derivative potentiometry and spectrophotometric titrimetry have been applied to the determination of carboxylic acids, sulphonamides, imides, thiols, phenols, and enols dissolved in solvent mixtures containing not less than 90% of acetone.²³ The preferred titrant is tri-*n*-butyl-methylammonium hydroxide and a list of suitable indicators for visual or photometric detection of the end-points is given. The determination of formaldehyde in technical hexamine is based on oxidation of the formaldehyde with Tollens' reagent containing a known amount of silver nitrate.²⁴ The excess silver is then titrated potentiometrically with a standard solution of potassium iodide. Hexamine does not decompose under these conditions. The titration of a number of amines in propionic acid—propionic anhydride mixtures using visual detection of the end-point has been described.²⁵ With a 1:1 solvent mixture or pure propionic anhydride, it is possible to titrate phenazone, caffeine or theo-

phylline with 0.1 N-perchloric acid using methyl violet, malachite green, Nile blue, neutral red, safranine, or sudan III as indicator. Amidopyrine can also be titrated, but with a limited number of indicators for end-point detection.

Sulphonamide derivatives can be characterised by means of the Schiff's bases formed by their interaction with halogen-substituted salicylaldehydes.²⁶ The 5-bromo-, 5-chloro-, 3:5-dibromo-, and the 3:5-dichloro-compounds are recommended as suitable reagents; they react quantitatively with aromatic amines on heating in ethanol for 10-30 min.

Vitamins

An ion exchange procedure has been recommended²⁷ for the separation of pyridoxine and ascorbic acid. Two columns are used, one on top of the other; the upper contains the weak base exchange resin, *Amberlite* IR-46, and the lower, the strong base resin, *Amberlite* IR-401. The solution of the sample (2-3 mg. of pyridoxine hydrochloride and 20 mg. of ascorbic acid) is added to the columns which are then washed with water. The upper column is then removed and the lower column is eluted with 0.1 N-hydrochloric acid to remove the pyridoxine which is determined photometrically with diethyl-*p*-phenylenediamine according to the procedure of Hrdý and Urbanová.²⁸ The polarimetry of ascorbic acid has been studied by Nebbia,²⁹ who recommends measuring the optical activity of the vitamin over a range of pH values and calculating the concentration from the data obtained. Optimal activity varies from +21° at pH 2.5 to +120° at pH 7. The polarographic determination of vitamin C in fresh fruit and vegetables using reduction with H₂S has been studied and the various factors influencing the determination have been established.³⁰ The results show that there is apparently no dehydroascorbic acid present in either fresh fruit or vegetables.

A new colorimetric determination of folic acid is based on the colour developed on boiling a solution of the substance with nitric acid and then treating with aqueous ammonia.³¹ The complex obeys Beer's Law and the extinction is measured at 485 m μ (blue filter). Coulometry or direct titrimetry with Chloramine T has also been recommended for the microdetermination of folic acid.³²

Antibiotics

A photometric procedure has been described for the determination of penicillamine, which is based on the blue colour formed when the compound is heated with iron (III) chloride and potassium cyanide at 65°. Measurement of the colour is made at 645 m μ and the amount of amino-acid is then determined by reference to a standard graph.

Another photometric procedure is used to determine the amount of ketonic substances in chloramphenicol,³⁴ reduction by the keto group of a mixture of phosphomolybdic and phosphotungstic acids results in the formation of molybdenum blue, which is measured at 610 m μ . The method is suitable for 50 μ g. amounts of ketonic substances in 0.1 g. of the antibiotic. Machek³⁵ has described the simultaneous colorimetric determination of chloramphenicol cinnamate and sulphonamides. The sulphonamides are first determined by diazotisation and coupling with N-1-naphthyl-ethylenediamine, the extinction being measured at 540 m μ . The antibiotic is then determined on another aliquot of the sample by reduction with sodium dithionite in alkali, followed by the use of the above colorimetric procedure. The coloured solution from the first determination is used as a blank.

The colorimetric determination of tetracycline with boric and sulphuric acids has been studied by Sekiguchi.³⁶ The method used is based on the procedure of Sakaguchi³⁷ for the determination of aureomycin. The new procedure is suitable for amounts of antibiotic in the range 5-35 μ g. per ml. Spectrophotometric methods are also recommended by American workers³⁸ for the determination of these antibiotics in pharmaceutical preparations. A method based on the reduction of Folin and Wu's reagents has been recommended for the determination of streptomycin and dihydrostreptomycin.³⁹

Andrew and Weiss⁴⁰ have extended their examination of the solubilities of antibiotics in various solvents; 22 salts of 14 new antibiotics are described.

Drugs

A method for the detection and determination of pyridine and its derivatives makes use of the colour change of red to violet when pyridines are treated in a buffer (pH 5) with cyanogen chloride formed *in situ*

from chloramine T and potassium cyanide.⁴¹ Nicotinic acid and its derivatives and *iso*-nicotinic acid all give colours, but the carbonyl derivatives of *iso*-nicotinic acid hydrazide require preliminary oxidation with cerium (IV). Isoniazid in the range 1-5 μ g can be determined. Sodium 4-aminosalicylate is determined colorimetrically by forming an orange-coloured complex with uranium (VI).⁴² The complex obeys Beer's Law over the range 0.75-6 mg. and has maximum absorption at 420 m μ . Isoniazid or *m*-amino-phenol does not interfere with the determination.

A coulometric method for the determination of cyclobarbitone and hexobarbitone is based on the addition of chlorine at a double bond.⁴³ The method is used on amounts of the two drugs in the range 1.2-3.2 mg. and accuracies of $\pm 0.7\%$ are obtained. Curry⁴⁴ has studied the forensic aspects of the identification of barbiturates. The mercury complexes of barbituric acid and its derivatives can be extracted into chloroform and the mercury then converted to the coloured dithizone complex. These reactions form the basis of a photometric method for the determination of a number of barbiturates.⁴⁵

Fine chemicals

A rapid method for the analysis of metol and hydroquinone is based on the fact that metol is insoluble in ethyl acetate.⁴⁶ The sample containing metol and quinol is shaken with ethyl acetate, then sulphuric or hydrochloric acid is added. The various layers are separated and titrated with cerium (IV) sulphate.

The colorimetric determination of camphor in camphor spirit uses *p*-dimethylaminobenzaldehyde as reagent.⁴⁷ The coloured product is examined spectrophotometrically at 460 m μ . This procedure is as accurate as the conventional gravimetric assay and is much more rapid. The main difficulty in the simultaneous determination of formaldehyde and paraformaldehyde is found to be due to the decomposition (depolymerisation) of the latter substance.⁴⁸ This reaches a maximum at pH 4.5 at 0°. The method now recommended uses dimedone to precipitate the formaldehyde in an acetate buffer at pH 4.6; the precipitate is filtered off and titrated with standard alkali; the paraformaldehyde does not decompose under these conditions. The

sum of the free formaldehyde and the polymer is determined by hypoiodite oxidation followed by iodometric titration.

The separation of phenol and cresol isomers by paper chromatography can be carried out on Whatman No. 1 or 4 paper using the solvent systems cyclohexane-chloroform-ethanol (9:1:0.6) and benzene-cyclohexane-methanol (2:24:0.25), and sulphanilic acid to reveal the spots.⁴⁹ A colorimetric method for *p*-cresol uses the formation of a reddish compound when the phenol is reacted with α -nitroso- β -naphthol and nitric acid in glacial acetic acid. The coloured solution has a maximum at 500 m μ which can be used to determine amounts in the range 0.4-50 μ g. per ml. No interference is experienced from phenol or *o*- and *m*-cresols.

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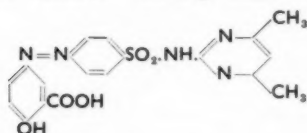
THERAPEUTICS

By S. J. Hopkins, F.P.S.

*Sulphonamides • Tranquillisers • Analgesics • Antimycotic
Antibiotics • Chlorprocaine • Hypertension • Cytostatics*

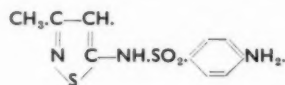
Sulphonamides

THE successes obtained with salicylazosulphapyridine (SP) in the treatment of ulcerative colitis led at once to a search for similar compounds, and Böttiger and Möllerberg¹ have reported their experiences with salicylazosulphadimidine (SD) and the corresponding sulphamethoxy pyridazine derivative (SMP). During trials in a



series of 14 patients, given doses of 1 g. four times a day, the blood concentration of the drug was five times greater with SD than with SP. This effect was considered to be due to the slow urinary excretion of the drug, and it will be recalled that the now almost obsolete sulphapyridine was excreted much more rapidly than sulphadimidine. In effect, this means that smaller doses of SD can be used to achieve the same levels as with SP, and this reduction in dose is accompanied by reduced side effects such as nausea and vomiting. Results with SMP were much less satisfactory, as toxic doses were necessary to obtain comparable blood levels.

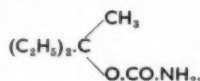
Some very interesting work with systemic sulphonamides has been the subject of a preliminary report by Adams and co-workers.² Although this group of drugs was introduced over 25 years ago, their potentialities are by no means exhausted. Following the introduction of the long-acting compounds, certain heterocyclic nuclei were used as substituents, particularly isothiazole. Promising results were obtained with the 5-substituted derivative, to which the name sulphasomizole has been applied. This compound exhibits a wide range of activity against a variety of organisms, and it diffuses well into



all body tissues, including the cerebrospinal fluid. It has the additional advantage of being well tolerated when given by intramuscular injection, and renal damage during excretion is unlikely. The report gives indications of synthesis, and further clinical investigations should produce interesting results.

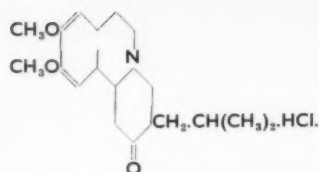
Tranquillisers

Following the introduction of meprobamate, many associated compounds have been investigated, and Melander³ has examined a series of tertiary alcohols and esters. The most effective compound had the following structure:



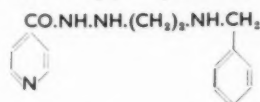
This substance, known as emyclate or nuncital, has twice the activity of meprobamate, and a more rapid effect. The drug has a selective blocking action on polysynaptic reflexes in doses that do not affect the monosynaptic pathways, and therefore has useful therapeutic applications. The synthesis of some of these compounds offers difficulties, but a suggested method is to react phenylchlorocarbamate with ethylmethyl propanol. Autoclaving the product under pressure with ammonia yields the required compound.

Further work has also been done on compounds related to reserpine. The tranquillising powers of this alkaloid are usually associated with the indole group, but in a new series of benzoquinolizine derivatives, which also have tranquillising properties, this group is absent. Quin *et al.*⁴ in reporting on tetrabenazine (2 - oxo - 3 - isobutyl - 9.10 - dimethoxy - 1,2,3,4,6,7, - hexahydrobenzo - a - quinolizine) found that this compound was more



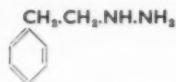
specific than reserpine. This effect was ascribed to a more rapid and more selective release of serotonin and noradrenaline, which occurred in the brain, but not in the peripheral tissues. This increased specificity and reduced duration of action has therapeutic value. Side effects are reduced and the compound, unlike reserpine, has little effect on the blood pressure. As many of the effects of reserpine have a peripheral and not central origin, the results with tetrabenazine suggest that the tranquillising effects of the alkaloid are not, after all, bound up with the indole group.

The discovery that the anti-tubercular drug, isoniazid, produced certain euphoric effects led to the introduction of the monoamine oxidase (MAO) inhibitors in the treatment of depression. The value of some of these early compounds was limited by side effects such as postural hypotension and hepatotoxicity, but Rowe⁵ and others, after investigating a large series of carboxamido alkyl hydrazines, found certain derivatives that were exceptional both in potency and lack of side effects. In particular, nialamide, or N - isonicotinoyl - N' - (β - N - benzyl carbamido - ethyl) hydrazine, was



selected for further study. During this work the potentiation of the action of barbiturates of the hexobarbitone type was considered to be an indication of hepatotoxicity, and the degree of reserpine antagonism and 5HT potentiation reflected the potency of the drug under review. On this basis the antidepressant action of nialamide appeared to be considerably greater than that of iproniazid. *In vitro* studies showed that the compound brought about an increased inhibition of monoamine oxidase, and although a causal connection between MAO inhibition and antidepressant activity still awaits proof, the therapeutic results give support to this promising line of research. Similar work on other compounds by Thal,⁶ who examined

eleven antidepressant preparations,

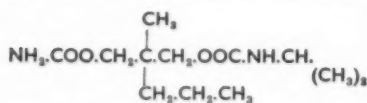


indicated that β -phenylethylene hydrazine also had exceptional properties. This substance, also known as phenelzine, is a powerful MAO inhibitor, and its value as an antidepressant has been confirmed by an extensive clinical trial. It has been compared with electro-convulsive therapy for rapidity of effect. Although chemically it has some relationships with the amphetamines, its influence on brain biochemistry indicates a fundamental difference in its mode of action. Tedeschi *et al.*⁷ have worked with 2-phenyl-cyclopropylamine (trans-cypramine), and suggest that the long action shown by some compounds is due to the destruction rather than the inhibition of the enzyme.

It is of interest to note that these new MAO inhibitors are also of value in angina. Iproniazid was originally used, but with prolonged therapy side effects were a limiting factor. MacKennon and Anderson⁸ gave Cavodil (β -phenyl isopropyl hydrazine) to a series of 28 patients, with striking improvement in some cases. The true value of any drug in angina is difficult to assess, as the condition is a subjective one, but the results are sufficiently favourable to warrant further trial.

Analgesics

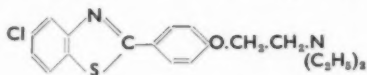
The mild relaxant properties of meprobamate can be modified very considerably by variations in chemical structure. Berger *et al.*⁹ have



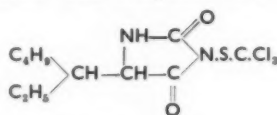
reported on N-isopropyl-2-methyl-2-propyl-1,3-propane diol dicarbamate. In this substance the hydrogen of one carbamyl group has been replaced by an isopropyl radical, and the new compound has analgesic properties as well as an atropine-like action on the central nervous system. Used therapeutically, it relaxes abnormal tension and relieves the pain of spasm in joints and muscles. This analgesic effect is associated with a modified central perception of pain without the suppression of natural reflexes.

Antimycotic

The variable response to many anti-fungal compounds affords both patient and dermatologist a series of occasions for hope. Any new compound is therefore of considerable interest, and 5-chloro-2-(*p*-diethyl-amino-ethoxyphenyl)



benzthiazole, reported on by Thorne and Harvey,¹⁰ has marked antifungal and antibacterial properties. This compound is of very low toxicity and its activity is increased in serum. It was used as a lotion, cream and powder in a strength of 0.5%, and appeared to be effective in a wide range of superficial fungal infections. Vaginal moniliasis is another therapeutic problem, but a fresh approach is the use of a hydantoin derivative,¹¹ 3-trichloromethylthio-5-(1-ethyl)-amyl-hydantoin or chlordanin. This compound is effective



when used as a cream or vaginal tablets. Being non-staining, it is readily acceptable by patients. Relief is experienced after two days' therapy, which should be continued for 14 days, but a second course appears to be necessary.

Antibiotics

Chloramphenicol is unique as the only antibiotic prepared synthetically on a commercial scale. Consequently, many derivatives have been prepared, but none has proved more active than the parent compound. The therapeutic activity of a substance is not a simple property, but is modified by solubility, excretion and degree of metabolic change. Thus chloramphenicol is rapidly inactivated in the body by conjugation with glycuronic acid, yet a basically weaker compound that escaped such inactivation might finally have a more powerful action. Working on these lines, Kunin and Finland¹² examined a number of derivatives of chloramphenicol in which the nitrophenyl group is replaced by others. Of particular interest are the 4-methylsulphonyl-phenyl and the 4-methyl mercapto phenyl compounds. These compounds were absorbed fairly well,

but the peak levels were achieved more slowly. Significant amounts of active substance were found in the urine, and this aspect has valuable therapeutic applications. The new compounds are more toxic than the parent drug, and further research is necessary but may prove rewarding.

Some very interesting work on the relative antibacterial activity of three available penicillins is reported by Garrod,¹³ following the introduction of a new derivative of the penicillin nucleus, namely the potassium salt of 6(α -phenoxypropionamido)penicillanic acid. This new compound—penicillin B—is stable against penicillinase, and should be active against those staphylococci which are resistant to penicillin G because of their ability to form penicillinase. Tested against such organisms, penicillin B proved more active than penicillin V, which in turn was more active than penicillin G, and the differences in activity were marked. When tested against streptococci and pneumococci, the pattern was different, penicillin G being more effective than penicillin V, with penicillin B as the least potent compound, but with relatively small degrees of activity between each. These tests confirm what has long been known about the differences in activity between penicillin G and penicillin V, and also reveal that these differences are greater and more important than previously suspected. Penicillin B is clearly the drug of choice in resistant staphylococcal infections, but is less active against streptococci and pneumococci. This however may be compensated by the higher blood levels obtained with the new drug. These results are of considerable importance, and may lead to a reconsideration of the form and value of sensitivity tests as now carried out.

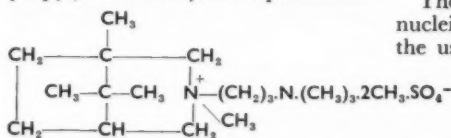
Chloroprocaine

Epidural anaesthesia is particularly useful in obstetric and gynaecological work, but the method has always lacked popularity. This is due mainly to certain difficulties of technique and to the lack of a suitable anaesthetic. The drugs hitherto employed have all had certain disadvantages, and the required compound is one that can be used in high concentration and in large volume, if necessary, without causing any toxic effects due to systemic absorption. Foldes and Crawford¹⁴ consider

that 2-chloroprocaine hydrochloride is such an anaesthetic. Their paper describes the results obtained in a series of 218 patients, using the drug as a 2% solution. Initial injections of 14-36 c.c. were given, followed if necessary by successive fractional doses to maintain the required degree of anaesthesia. Chloroprocaine has a more rapid action than procaine and has double the anaesthetic potency. Like the parent compound, it is hydrolysed by cholinesterase but at a more rapid rate, and as there is no accumulation in the tissues the toxicity is low. The drug has no value as a topical or surface anaesthetic.

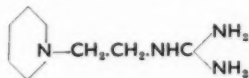
Hypertension

The use of blocking agents in the treatment of hypertension is extending very rapidly. Every drug so far available is, for certain patients, almost the drug of choice, but Smirk,¹⁵ in reporting on trimethidinium methasulphate, considers that a compound consistent in dose and action, and suitable for the majority of patients, has yet to be introduced. The majority of compounds hitherto available are either quaternary ammonium substances or secondary amines, and certain differences between the two groups can be noted. The quaternary ammonium compounds are not regularly or completely absorbed when given orally, and toleration may occur during prolonged therapy. The secondary amine substances are absorbed more completely, and toleration is rare. The new compound, N(trimethylammonium propyl) - N - methyl - camphidinium



methosulphate is an asymmetric bis-ammonium compound, and appears to possess some of the properties of both groups. It was originally described by Klupp,¹⁶ and was reported on by Dunsmore *et al.*¹⁷ who found some evidence of drug tolerance. This effect was not confirmed by Smirk, and in a series of 32 patients he found that only five preferred other forms of treatment. The new compound resembles the quaternary derivatives in its incomplete absorption, and the secondary amines in causing little toleration or toxicity during long-term therapy.

The effects of the drug appear to be due to both a ganglionic blockade and a central action, and can be potentiated by chlorothiazide. The value of these ganglion-blocking agents is limited by the undesirable effects on the parasympathetic ganglia, and the introduction of bretylium tosylate (see Progress Report, March 1960, p. 121), which has a blocking action on peripheral sympathetic nerves, marked a new approach to the problem. Further developments on these lines has been reported by Leishman *et al.*,¹⁸ using



2 - perhydroazocin - 1' - yl - ethyl guanidinium sulphate, or guanethidine. This substance represents a new class of medicinal substances, and although unrelated chemically to bretylium, it acts similarly by a selective inhibition of the post-ganglionic sympathetic nerves. The drug appears to act by preventing the release of the impulse-transmitting substances at the myoneural junction, as the receptor sites remain unaffected. Guanethidine differs most sharply from bretylium tosylate by its prolonged action, which permits single daily doses. In a series of 25 patients with varying degrees of hypertension, Leishman and his associates found that the majority could be stabilised on a daily dose of 30-60 mg. On this regimen a gradual and progressive fall in blood pressure took place.

Cytostatics

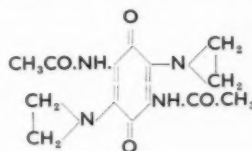
The importance of pyrimidines in nucleic acid metabolism has led to the use of various analogues in the treatment of cancer. Heidelberg *et al.*¹⁹ have suggested that these analogues, like azaguanine and 6-mercaptopurine, might act by being incorporated into nucleic acids, or by having a blocking action on various precursors. Gold *et al.*²⁰ have used various uracil derivatives in this way, the most active substance tried being 5-fluorouracil.



It is of interest to note that 4-fluorocytosine, which differs only in having an amino-group instead of an

hydroxyl-group in the 4-position, is inactive. The value of 5-fluorouracil as a therapeutic agent is limited by its toxicity. Toxic reactions can be reduced by oral administration, as there is no relationship between toxicity and activity, but further work on reducing side effects is required. A very different approach to the problem is reported by Malak,²¹ who used an oral preparation containing the aldehyde derivatives of polyoxymethylene glycol. The best results were obtained in malignant epithelial tumours, as other drugs are often of little value in this condition. The compound has an additional interest as an example of aldehyde therapy.

A number of quinone compounds have also been investigated as anticancer compounds, and 2-5-bis-(acetamido) - 3-6-bis (ethylene-imino) 1-4-benzoquinone has been reported on by Boiron *et al.*²² This



substance was well tolerated by the majority of the 65 patients taking part in the trials, but apart from a few encouraging results, the response was not exceptional. This may be associated with too low a dose of the drug, as the substance has also been examined by Bernard *et al.*,²³ who also tested the corresponding 2-5-bis-methoxyethoxy compound. These workers obtained the best results in treating Hodgkin's disease and other haemopathies, and considered it to be the first compound effective in certain lymphosarcomas. In carcinoma the results were unimpressive and of little value.

In another field some results obtained by Stone *et al.*,²⁴ in the chemotherapy of Ehrlich's ascites tumour have a considerable speculative interest. It has long been known that large quantitative differences exist between the oxidative capacities of normal and tumour cells, and this forms a possible basis of chemotherapeutic attack. Cyanide, for example, has a definite inhibitory effect on malignant tissues, but is too toxic. Animal experiments have shown that survival times following the intrapleural injection of dilute cyanide solutions can be extended significantly if the animals are previously anaesthetised by ether. The

hyperglycaemic action of ether is well known, and it may be that this effect is associated with an increased susceptibility of certain enzymes to the blocking action of cyanides. This has interesting potentialities when considering the design of cytostatic compounds.

Another approach of considerable theoretical interest is that of Peck *et al.*²⁵ These workers have suggested that the nitrogen mustard analogues of certain antimalarials might be of value as cytostatic drugs. From the known tissue distribution of some antimalarials there appears to be a definite tissue localisation, and this is supported by the fact that some compounds depress the activity of the bone marrow. Peck *et al.* consider that the substituted quinoline nuclei of such compounds could act as carriers for the *bis*-(2-chloro-ethyl)-amino group of the nitrogen mustards, with a possible increase in activity. This paper gives useful methods of synthesis for this type of compound.

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Pest Control Chemicals

By D. P. Hopkins, B.Sc., F.R.I.C.

*Onion fly control • DDT's effect on barley • Granular weedkillers
Fruit and weedkillers • Dalapon • A new weedkiller • Silica insecticide • Solvents for pesticides • Pyrethrum • Pesticides as bird scarers*

Onion fly

PERIODICALLY attacks of onion fly in Britain reach epidemic proportions and crop losses—including leeks and shallots—are then extremely high; 90% onion crop losses can occur. Traditional methods of protection are inadequate in "plague" years. A Scottish paper¹ reports valuable progress in developing a seed dressing treatment. Initial tests showed that gamma-BHC was more phytotoxic to onion seed and seedlings than endrin or dieldrin; however, these last two insecticides would have to be effective at less than 3% by weight of seed to avoid phytotoxic hazards. Pilot field-trials with gamma-BHC, dieldrin, thiram and calomel were then carried out. The first and last were discarded for cost and phytotoxicity reasons respectively. Dieldrin led to the highest yields of saleable onions, but the best control was obtained with a combined use of dieldrin and thiram. Although thiram alone at 1.5% proved valueless and even dieldrin at only 2% was of little use, a combined dressing of the two, each at a lower amount, proved extremely effective, a dressing of 1% thiram with 1.5% dieldrin giving a yield of 920 oz. of onions per like plot compared with 586 oz. for a 2% dieldrin treatment. The influence of thiram seems one of activating or synergising dieldrin's fly toxicity, and this may well be usefully developed for other types of dieldrin seed dressing. The onions grown were tested by cooking and tasting and no taint or colour or texture defects were found.

It is interesting that earlier work^{2,3} on control measures for cabbage root fly damage to turnips found that little control was given by seed dressings at 1 oz. per lb. of seed of a mixture of 75% dieldrin and 10% thiram: also that poor control was given when gamma-BHC took the place of dieldrin in the thiram-

combined treatment. For this somewhat similar crop hazard, the most hopeful control was obtained by spraying the young and developing crop with a 0.1% dieldrin spray.

DDT and barley

Recent work in Wales⁴ has shown that barley reacts to DDT spraying in a most unusual way. Some varieties are unaffected, others severely damaged—chlorosis, cessation of leaf-growth, and high loss of yield being the main consequences. The variety most used today, Proctor, is fortunately immune, but Freja, Rika, Herta and Ingrid are among the susceptible varieties. Nevertheless, tests with other chlorinated hydrocarbon insecticides have not shown similar reactions for barley varieties. DDT spraying reduced the yield of Rika by 36% for one spraying and by 72% for three sprayings. This reaction to DDT is unusual for any crop, and more unusual in that the susceptibility is genetic. It is not a discovery of purely academic significance. Though cereal crops are not commonly sprayed with DDT, mixed corn crops often must be to control the attacks of frit fly on oats. If DDT is used, the barley variety sown in the seeds mixture must be DDT-resistant. However, the scientific value of this new work could be indirectly important. DDT-resistant strains of mosquitoes, flies, etc., owe their immunity to an enzyme that converts DDT into the relatively harmless DDE. It has been argued that the existence of this enzyme is due to a single gene—and it would seem now that a single gene gives some barley varieties resistance to DDT. Is the same enzyme operating in both the plant and animal kingdom?

Weedkiller granulation

A survey of progress so far made in developing granular weedkillers has appeared in the U.S.A.⁵ In

general, sprayed applications give far better control over established weeds, but in certain cropping circumstances—mainly when the soil is initially weed-free—granular application has potential advantages. A larger amount of the active ingredient reaches the soil than is the case with spraying, and this is an important factor in controlling weeds that grow under the cover of crop foliage. The granular method of presentation tends to increase the inherent selectivity of a weedkiller. The actual formulation of granular products is a field still requiring much more investigation. Some carriers adsorb the active ingredient and its solvent too tenaciously. This tends to be true for many of the more adsorptive carriers, and those which are less adsorptive, though they readily release the weedkiller when in the soil, are, quantitatively, poor carriers.

Weedkillers for fruit growers

Another survey of present progress⁶ has dealt with weedkillers for British commercial fruit growing. For raspberries, control of meadow and couch grasses can be achieved by dalapon if this is given in December—later use led to cane injury and loss in yields. There is a risk in this treatment, but it must be balanced against the risk of crop loss through grass infestation. Winter use of MCPA has controlled creeping butternut without injury to raspberries. IPC (propham) and CIPC also gave control without deleterious effects. Simazine and monuron have given long-term control over mixed weed infestations, the former with safety even when applied in the growing season. Both these weedkillers seem likely to keep raspberry plantations reasonably weed-free during much of the growing season—and this could bring considerable labour economy to the industry.

For strawberries, mixtures of 2,4-DES and propham can be safely used during the growing season. Simazine, however, has caused some damage to plantations if applied before the strawberry plants are fully developed. More investigation of simazine's use for this crop is required. For blackcurrants and gooseberries, results for winter-applied weedkillers are much the same as those already mentioned for raspberries. Gooseberries are more sensitive to dalapon than blackcurrants.

The general conclusion of this detailed paper is that a number of

selective weedkillers can now be confidently recommended for weed problems in commercial fruit growing, but there remains an experimental element in all such usages. Effects of soil type or fruit variety, for example, are still requiring wider study. Consultation with local advisory officers is prudent before deciding to use any particular weedkiller.

Dalapon research

Using sodium 2,2-dichloropropionate (sodium dalapon) prepared as a carbon-14 radio-labelled substance, the uptake of this weedkiller by two crop plants, corn and the soya bean, has been studied.⁷ Radio-activity entered the plants whose roots had been exposed to dalapon. It became distributed throughout the plants with higher concentrations in the younger tissues. It also entered the soya bean plants when spotted on the leaf, and here also younger tissues had the highest concentrations. Paper chromatographic examination of extracts could correlate the radio-activity with actual presence of dalapon as such, and no breakdown products of dalapon were found. It would seem, therefore, that dalapon's lack of effect upon the selectively immune crop plants is not due to breakdown mechanisms within such plants.

Data showing the low oral toxicity of sodium dalapon to laboratory animals and cattle have been obtained.⁸ Dogs were given 100 mg. per day for a year and rats half this daily amount for two years; there were very slight effects upon kidney weights. Dogs and rats fed smaller daily amounts for similarly long periods were no different from controls. Cattle could tolerate large doses without serious effect. The chance of residues affecting human health or wild life is regarded as minute. Physical contact with the pre-diluted material may be more troublesome. Undiluted sodium dalapon can cause skin irritation if allowed to stay on the skin for a long period; in solid form or in strong solutions it can cause pain and irritation to eyes, but without seriously damaging consequences.

A new weedkiller

Dutch workers have described experimental work indicating the promise of a new weedkiller, 2,6-dichlorobenzonitrile or H 133.⁹ It has been found to be especially

effective in inhibiting weed seed germination, and it is easily absorbed by seeds from the vapour or from solutions. It has good phytotoxicity to a range of weeds including wild oats, bracken and chickweed. Seeds of some crop plants have good resistance to it, e.g. rice, corn, sunflower. It is also said to have low toxicity for warm-blooded animals.

Silica as an insecticide?

A pure white micro-fine amorphous silica is being marketed as an insecticide in the U.S.A. under the name *Silkil*.¹⁰ Claims presented are rapid lethal effect, e.g. 30 min. for ants, 2 hr. for roaches; prolonged residual effect as there is no loss of activity over months; freedom from injurious side effects, for such materials have long been used as talcums. Also, the effect being physical, it is argued that insects will not build up resistance. It is non-phytotoxic, though some injury occurred to glasshouse roses under very heavy dew conditions. A wide range of insect pests—from fleas and silverfish to red spider mites on greenhouse plants—is included in the various U.S. registrations already secured for *Silkil*. Control of soft-bodied sucking insects like aphids is poor; scaled insects seem to be most vulnerable. According to the type of insect there are three grades, distinguished by weights per cu. ft.—4 lb., 12 lb. and 22 lb. The lighter grades are used mainly for household types of insect and the last and heavy grade has been developed for agricultural uses.

Solvents

The oil industry has increased its output of aromatic hydrocarbons in recent years and this has widened the range of solvents available for spray formulation.¹¹ Supplies are now so good that any manufacturer should be able to choose a low-cost solvent. The characteristic that requires most careful evaluation is phytotoxicity. For this, field tests rather than greenhouse tests are recommended. Tests are described which showed that for corn heavy aromatic naphthas were unsuitable and xylene types much safer. It is contended that no single solvent is "ideal" for all the liquid products a manufacturer may be making; also, that provision of data about phytotoxicity should be the responsibility of the solvent supplier and not of the formulator.

Pyrethrum

A study of pyrethrum synergist development with particular reference to sulphoxide¹² makes the point that throughout synergist research work little has been done to determine an optimum effective ratio for synergist/pyrethrins. Such an attempt—for sulphoxide and for one insect species—is described. Using the Peet-Grady method a curve for LD₅₀ values is obtained, plotting percentage contents of sulphoxide vertically and those of pyrethrins horizontally. From such a curve the optimum concentrations of sulphoxide can be read for any pyrethrin concentration within the range of the experimental work. Besides this special feature in the paper, there is a thorough review, with many references to the literature, of sulphoxide as a synergists.

Another paper¹³ has compared four synergists for pyrethrum using houseflies, weevils and flour beetles. The synergists were piperonyl butoxide, S. 421, sulphoxide and bucarpolate. The potencies varied with the test insect and changes in the synergist/pyrethrins ratio did not materially alter these relative differences of potency. Thus, for houseflies the order of potency was: piperonyl butoxide, 1; sulphoxide, 1.1; bucarpolate, 0.7; S. 421, 0.4. For flour beetles, it was, in the same order of synergists, 1; 1.8; 0.7; 0.6. For weevils (two species) sulphoxide and piperonyl butoxide were equal in potency and the other two were much less potent. S. 421 is octachlorodipropyl ether; bucarpolate

is the piperonylic acid ester with monobutyl ether of diethylene glycol.

A new and fairly rapid method for determining Cinerins I and II and Pyrethrins I and II in pyrethrum preparations has been described.¹⁴ It is based upon quantitative preparations followed by chromatographic separation of the 2,4-dinitrophenylhydrazones of the active constituents. These can be separated on alumina columns.

Insecticides won't kill birds

In a study¹⁵ of damage to fruit tree and fruit bush buds in the dormant season, mainly attributed to the attacks of bullfinches, one method of control tested was that of chemical repellents. Twenty-one possibly repellent chemicals were tested in 39 forms, the work being done on 10 farms in Kent and East Sussex. The chemicals were: aldrin, alum, anthraquinone, BHC, Bordeaux mixture, camphor, dieldrin, gentian violet, grease - banding materials as smears, hydrated lime, lime sulphur, mercaptobenzthiazole, naphthalene, β -naphthol, paraffin emulsion, pepper extract, sodium thiocyanate in petroleum, tar oil emulsion, and proprietary repellents of unknown composition. Except for greases, none of the materials applied was effective. Anthraquinone appeared to give some protection to pear trees for a few days. All greases tried gave a high degree of protection—almost complete or in fact complete—but unfortunately they have severe phytotoxic effects upon the trees, particularly bark damage

in the form of corky growth and reductions in the number and size of leaves.

The failure of so many chemicals, including well-known insecticides used for crop protection, is significant in another context. Newspapers frequently publish letters accusing pest control chemicals of injuring or killing wild life and birds are often cited as victims. Yet here is proof that some typical products failed even to repel birds. These facts should be rammed home by the Association of British Manufacturers of Agricultural Chemicals.

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CHANGES IN PHARMACEUTICAL PRODUCTION (Continued from page 285)

Control

The tendency today, and one that will grow, is for a member of the control staff, a sampling officer, to draw samples of packaged goods and submit them to routine analysis, but this alone is not the answer. In many cases there is no substitute for a local laboratory in a manufacturing department making continual checks on the process as an aid to production quite independently of quality control of the finished products line. In America it is more common than in this country for the analytical section responsible for quality control of the finished product to report only to the managing director or his equivalent. Although practice in this country appears variable and less stringent, I can foresee the development here of both systems, that is ultimate analytical control and departmental manufacturing control growing side by side.

Just as the scene in the production department may change with the introduction of a local control unit, so within the field of analytical control the scene is changing, traditional chemical determinations giving way to the much more rapid physical methods, for example, rapid alkaloidal determinations with a polarograph.

The future

Some pharmaceutical houses already specialise in what might be called public specialities: they advertise to the public products which are rarely prescribed and they have few, if any, ethical items in their lists. Other companies have a reverse situation in which virtually all their products are available only on prescription. Will this tendency to specialisation increase and what will be the effect? Will it, as with one proprietary product, lead to real mass production, fully automated, where the ingredients are continually weighed, batch mixed using an interrupter device, and then fed into a continuous filling unit?

Will there be more official control on multiplicity of formulated products and if there is, what will be its effect on production methods?

Will the responsibility for clinical evaluation of drugs in the future shift from the discoverer to some other body, and will the production pharmacist as a result be under even higher pressure to get his product produced, packed and in the market when the ultimate time of release comes?

PLANT AND EQUIPMENT

►DUST CONTROL

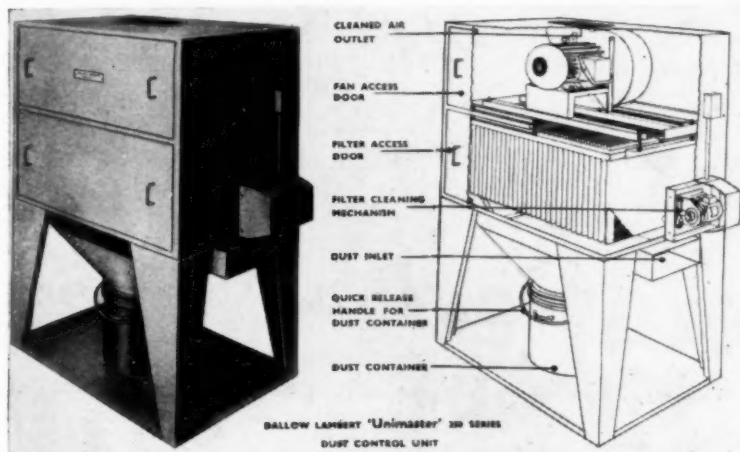
Dallow Lambert have introduced the *Unimaster 250* series dust control unit which follows the 70, 100 and 150 series, already in production. This larger capacity collector with 250 sq. ft. of filter cloth area is designed for dealing with heavier dust concentrations. It is suitable for heavy duty individual machines or with advantage can be used as a small multiple connection plant, having low initial and running costs in comparison with equipment that is specially designed and tailor-made for a specific application. Runs of ducting can be attached to this collector; if an installation is dis-banded the collector is re-usable on another application; alternative fans and motors, filters and dust containers can be supplied from a standard range.

►MICRO-OVEN

A handy oven is now available for small-scale work and for semi-micro analysis. The micro-oven consists of an anodised aluminium outer casing—to withstand corrosive atmospheres—and an inner metal casing forming a cylindrical cavity 4 in. deep × 4 in. diameter. Fitted to the double-walled lid there is a small tray which locates in the centre of the cavity as the lid is placed on the mantle—venting holes are provided in the base and in the lid, with a second hole for



Oven for small-scale work and micro-analysis.



Heavy duty dust control unit with 250 sq. ft. of filter cloth area.

a thermometer. High temperature lagging 2 in. thick provides good thermal efficiency and temperatures up to 300°C. can be quickly reached although the loading is 200 watts only. The price is £12. Manufacturers: Isopad Ltd.

►BENZOLE FRACTIONATION UNIT

A new continuous benzole refining plant, designed and constructed by the A.P.V. Co. Ltd., has been put on stream at the Scunthorpe coke oven and chemical plant of the Appleby-Frodingham Steel Co. (Branch of the United Steel Companies Ltd.). This plant is the first one in Britain to produce nitration grade boiling range benzole and toluole, 2° xylene and 160/190° naphtha continuously from crude coke oven benzole. The design throughput is 5½ million gal. p.a. A striking advance in the benzole refining field is the operation of five continuous fractionating columns in series.

In a test run it was established that at a throughput rate of over 650 gal. per hr. of crude benzole the refinery produced the above products with a steam consumption of less than 11.8 lb. per gal. of crude. Subsequent operation shows a considerable reduction in this figure.

The refinery incorporates the new APV continuous deffronting unit which is capable of producing deffronted benzole containing as little as 1 p.p.m. of carbon disulphide

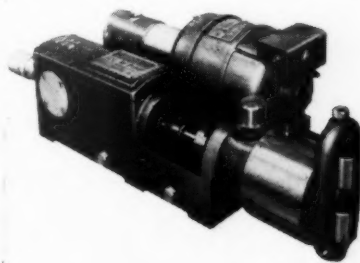
sulphur with a very low loss of benzene in the overhead fronts.

This is the second benzole refining unit supplied to Appleby-Frodingham by APV. The first, erected in 1940, processed over 38 million gal. of crude benzole and has now been superseded by this latest plant of twice the original capacity.

►HIGH PRESSURE PUMP

To meet demand for metering pumps of small capacity but of a high degree of metering accuracy and without glands on the pumping side, the Distillers Co. have developed a diaphragm pump with the characteristics which meet these requirements.

The fundamental mechanism of the well tried D.C.L. "M" pump has been built into a high-pressure diaphragm head unit and tests have shown high accuracy with a pump tested at 2,500 p.s.i.g. with the very



D.C.L. high - pressure metering pump.

small maximum capacity of 700 ml./hr. At this pressure the compressibility of the hydraulic fluid which operates the diaphragm and the compressibility of the fluid being pumped are significant but calculable, and when these factors are taken into account the necessary allowance can be made by choosing the appropriate micrometer setting for the required delivery capacity and the characteristic straight line calibration of range of D.C.L. metering pumps is retained.

The price of the new pumps is dependant to some extent upon the materials of construction and pressure-capacity requirements. A unit with stainless steel head, as illustrated in the photograph is approximately £160.

►PACKAGED CHEMICAL PLANT

In the last few years, Premier Colloid Mills Ltd. have adopted the "packaged" principle in the design and construction of small chemical plants involving the use of colloid mills, and a number of specialised plants have been sold for the production of dispersions and emulsions. Units recently built cover plants for the manufacture of greases, paraffin wax emulsions, ice cream flavourings, cosmetic creams and emulsion and oil paint. The plants consist of premixing vessels with mixers, mills, pumps and finished product tanks, all mounted on a common base plate. Water and steam pipework is all built-in, as is all the electrical wiring. These services are then taken to one central point for connection to external services. Added advantages of this method of construction are that the first cost virtually covers the complete capital outlay since no hidden extras are involved in assembling the plant. The installation of such plants in under-developed countries overseas has many advantages.

Chemical Engineering Premier Ltd., a subsidiary of Premier Colloid Mills Ltd., has been formed to handle the development and sale of packaged plants. Mr. D. T. Alderman, chief engineer of Premier Colloid Mills Ltd., has been appointed director and general manager of the new company.

For more information about the plant and equipment described please use the coupon on page 324

"Beatall" electrically operated label gumming machine.

►LABEL GUMMING MACHINE

Recently re-designed, the *Beatall* range of label gumming machines are made in five sizes, having roller widths of 6 in., 8 in., 10 in., 12 in. and 14 in. respectively.

They have been designed to meet the need for reasonably constant use on applications of before and up to the need for fully automatic and specialised machines and will handle labels of any size or shape within their compass.

Label sizes are governed by the maximum roller width of each model, length being up to reasonably handled proportions, there being no adjustments necessary for the different sizes. Each model is supplied complete with an enclosed drip-proof $\frac{1}{2}$ h.p. geared motor and top mounted switch, the whole assembly together with gum box, feed and delivery units being mounted on a solid one-piece base, the only addition necessary being a suitable length of flex together with a 3-pin 5 amp plug, for immediate operation.

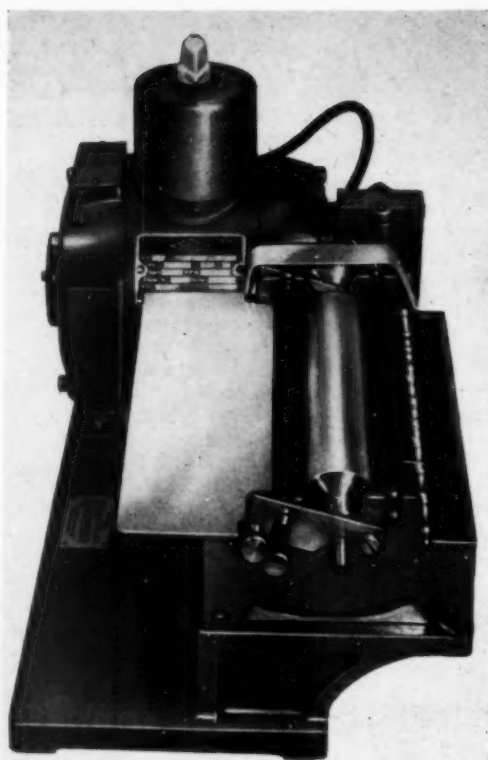
Farrow and Jackson Ltd., besides producing *Purdex* gum for this machine, now have a special paste for use with the *Beatall* which may also be used, when it is required, for applying labels to tins.

►CHEMICAL PUMP

The *Perfecta* pump marketed by Mason and Morton Ltd. is of the centrifugal single entry type with a closed impeller. It is glandless, so there are no leaks; hence it is ideal for toxic fluids, all acids, radioactive fluids, hygienic conditions, etc.

Its distinctive features include:

1. Self lubrication (by pumped fluid) of plain shell bearings.
2. No bedplate or any support apart from the pipe line itself (only above 5 h.p. is a supplementary support recommended).
3. Fits into line regardless of angle or direction of slope. Shaft of



pump can always be maintained in a horizontal plane.

4. Dismantling for inspection or replacement of mechanical parts can be done without breaking the line.
5. Separation of electrical and mechanical sections to avoid trade union disputes.
6. Maintenance limited to a check-up once every 12-15 months approx.
7. Models available for operating temperatures from -40°C. to $+400^{\circ}\text{C.}$
8. Materials of construction to client's specification.
9. Suitable for static pressures of up to 700 p.s.i.a. and delivery pressures of up to 85 p.s.i.g.
10. Competitive price and short delivery for both the two- or four-pole speed types.
11. Stator easy to rewind locally if necessary.

►BETTER GLASSED STEEL

Enamelled Metal Products Corporation (1933) Ltd. have greatly increased the thermal shock-resistance of their new Pfaunder Glassed Steel 59. It is said to show an improvement of 30% over conventional glassed steel under the most severe shock treatments caused

by the meeting of unexpected or unavoidable temperature differentials. At a temperature of 450°F. it can withstand the thermal shock of ice water at 32°F. without any sign of chipping or weakening; and under certain conditions an acid can be raised to 450°F. without damage.

The safe Delta T for Glassed Steel 59 at a normal vessel operating temperature is 260°F. (formerly it was 200°F.). At the peak operating temperature of 450°F., the safe Delta T is now 150°F. (It used to be 115°F.)

When a problem covers thermal shock from the jacket side of the tank, the figures can be higher, because the steel thickness absorbs some of the shock effects.

The microstructure of glassed steel 59, which is responsible for the improved thermal shock-resistance, also allows lapping of nozzle faces on all nozzles up to and including 8 in. in diameter.

There is no additional cost for glassed steel 59 on all Pfaudler standard equipment, which includes storage, processing and reaction vessels for high and low pressures, condensers, receivers, evaporating pans, transport tanks, pipes and valves.

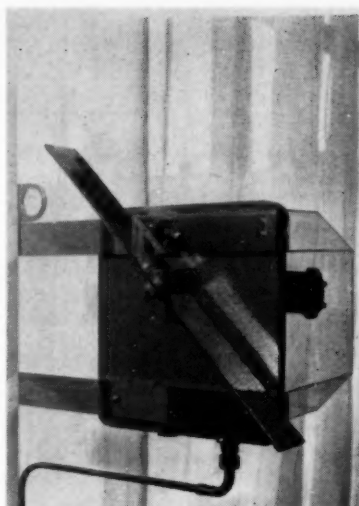
►BIN-LEVEL CONTROLLER

A new type of bin-level controller, to regulate and indicate the level of materials in bulk storage containers, has been marketed by Henry Simon Ltd., Stockport, after extensive testing in various industries. Its main advantages are:

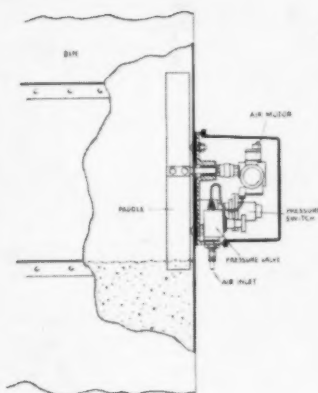
1. It is operated by compressed air, an important factor where electric circuits are undesirable.
2. It can be used with most types of solids or liquids, including



Pfaudler glassed steel 59 at 230°C. withstanding the shock of ice water at 0°C.



Left: Bindex level controller—a demonstration model with transparent casing. Right: A diagram showing the method of operation.



cohesive materials such as flour or cement for which some existing instruments are unsuitable.

3. It is inexpensive to buy, simple to install, simple to maintain and is thoroughly dependable.

Known as the Bindex pneumatic bin-level controller, the instrument consists of a small (about 9 in. square) casing which houses a pressure valve, a pressure switch and an air motor. Outside the casing is a simple paddle (normally 16 in. long) which is connected to the air motor by a spindle. When the Bindex is in position, the spindle passes through the bin wall or roof, the casing being outside the bin and the paddle inside. The paddle oscillates under air pressure with a continuous see-saw motion, a movement which is hampered or stopped when the level of the bin contents reaches the instrument. Interference with the movements of the paddle immediately activates the pressure switch which operates a light, sounds an alarm or initiates controlling action to the equipment feeding the bin. The pressure valve can be finely adjusted to give instant reaction even on a stock which offers little resistance to the paddle movement.

The Bindex is suitable for use with a wide range of materials and is at present operating with rubber pellets, flour, wood flour, ceramic dust, cement, starch products, resins, plastic powders and granules.

Henry Simon Ltd. offer a free testing service on customers' materials in their laboratories.

►ALL-GLASS PUMPS

Two all-glass centrifugal pumps for dealing with corrosive liquids were demonstrated recently in the chemical engineering department of the Imperial College of Science and Technology, South Kensington, by QVF Ltd. Describing the pumps, Mr. Brian H. Turpin, managing director, said: "Over two years' work on design and development have been devoted to their production. We are confident not only of their ability to resist all corrosion caused by the fluids they handle, but also of their impressive mechanical performance."

The glass impeller is of simple design based on a vortex-type inlet with specially designed arms. The mechanical seal is a glass-loaded Fluon bellows rotating on a glass plate, while a specially designed bearing chuck holds the precision-ground impeller shaft. The pumps, which are mounted on heavy cast-iron base plates, require priming.

The following figures are for performance when pumping cold water.

GPA/6	
Gal. per min.	Total head feet
10	24
30	20
50	13

GPA/9	
Gal. per min.	Total head feet
20	45
40	41
60	35
100	25

BOOK REVIEWS

Vitamin B₁₂

By E. Lester Smith. Pp. xii + 196. Methuen, London. 1960. 15s. net.

This is an admirable little book. It is amazing that so much matter has been compressed into such a small space. The style is very readable and the whole subject logically developed.

The first chapter describes the investigations which led to the discovery of vitamin B₁₂ and its characterisation as a definite chemical entity. This is followed by an account of the distribution of the vitamin in nature. The third and fourth chapters, which describe the isolation of the vitamin and the determination of its complete chemical structure, are particularly well done and very clear. There are also chapters on the biogenesis of the vitamin, derivatives, analogues and methods of assay. The remaining chapters discuss such subjects as binding factors, especially the intrinsic factor, absorption, excretion and distribution of the vitamin in the body, diagnosis and treatment of megaloblastic anaemia, the function of the vitamin in animal and human nutrition, and finally possible mechanisms of action.

This monograph can be unreservedly recommended as an authoritative account of vitamin B₁₂ and the author is to be congratulated on the production of such a masterly review of the subject. In the circumstances, therefore, it is painful for me to have to point out to Dr. Lester Smith that he has fallen short of perfection by omitting an authors' index. I trust this omission will be rectified in another edition.

E. BARTON-WRIGHT.

Industrial Gums: Polysaccharides and their Derivatives

Edited by R. L. Whistler, assisted by J. N. BeMiller, Academic Press, New York and London. 1959. Pp. 766. £8 18s. 6d. net.

THERE are 31 chapters by various contributors constituting in the editors' words "a collection of practical information on industrial gums, prepared in such a way that it may be useful to research workers, chemical engineers, technical sales personnel and legal people who wish to

learn more about gums." The coverage of materials is extensive, ranging as it does from the starches at one extreme to "some lesser-known seaweed extracts" at the other. As the title implies, the book does not set out to discuss the intricacies of structural formulae in detail, but it does give overall pictures of the various gums in respect of their production, uses and properties.

It is a reflection of the progress in this field that almost a quarter of the book is concerned with the newer carbohydrate products made either by separation from natural mixtures (e.g. starch amylose) or by chemical reaction (e.g. starch ethers).

D. A. SUTTON.

Chemistry of Plant Gums and Mucilages and some Related Polysaccharides

(American Chemical Society Monograph No. 141.) By F. Smith and R. Montgomery. Reinhold, New York, and Chapman & Hall, London. 1959. Pp. 627. £7 4s. net.

THIS book will undoubtedly be regarded as a standard work, splendidly written as it is by two authorities in the field. It has long been clear that investigators in the plant gum field had established techniques which enabled most new gums to be shaken down to their bare bones in a very short space of time. The details of how to do this occupy the first half of the book and the structures which have been deduced occupy most of the second half. It is refreshing to see a chapter, however short, on the physical properties of gums and mucilages and the authors' statement of the large gaps which remain in this sector. The unusual Formula Index is a lesson in simplicity and teaching method.

D. A. SUTTON.

Translation from German for Chemists

By H. H. Neville and W. E. Shute. Blackie, London. 1959. Pp. 139. 15s. net.

THE notorious lack of linguistic ability amongst British scientists is well known and beginning to worry the scientific authorities. During his university training every science student is obliged to acquaint himself with a working technical knowledge of at least two European languages. This may satisfy the consciences of Deans of Science Faculties, but the net gain by most scientists after graduation is very small. What is this due to? Most people will readily ascribe it to the lack of linguistic ability of the Anglo-Saxon people, who have no need to learn foreign languages as long as foreigners prefer to speak English. In contrast to this the Dutch and Scandinavians must of necessity speak two or three foreign languages, which fact is constantly impressed on English scientists at international conferences. Yet it must be remembered that the German language, which is spoken and understood throughout Germany, Austria, Switzerland and Central Europe, has a vast scientific tradition and no scientist worth his salt can afford to ignore it.

The book here reviewed tries to bridge this gap by presenting a short course in basic German for the chemist. The authors have clearly stated that they assumed no previous knowledge of German, and have suggested that the reader who works through this book systematically should be able to translate texts set in examinations for science degrees as well as most scientific journals. The approach represents a fusion of methods developed independently by the authors, who are a chemist and German scholar respectively. The book is divided into 18 chapters, each chapter dealing with a different grammatical case, and after every few chapters some translation practice is interspersed. Altogether it is packed with useful grammatical matter and undoubtedly if studied consistently would yield a smattering of technical German.

I. L. HEPNER.

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NEWS . . .

Chemicals: "an adventure in working"

LAUNCHED at a time when many young people will be leaving schools and universities and thinking of their careers, a new booklet "The Chemical Industry—a Career for You" has been issued by the Association of British Chemical Manufacturers. It is a recruiting booklet in the modern style—factual, concise and lavishly illustrated. Sir William Garrett, chairman of the Association has the first word. "To young people with an eye on the future and prepared to accept its challenge, the chemical industry is a gateway to opportunity," he declares.

First the chemical industry is explained in brief in all its ramifications—from plastics to photographic chemicals. Then the phenomenal growth of the industry—doubled in size in ten years—is stressed. Working conditions and the opportunities for skill and talent are then explained. Finally, with diagrams and words the career opportunities "an adventure in working" are explained.

Tucked into a pocket in the cover is a 40-page appendix in which chemical firms list the opportunities they offer.

Fisons seek markets in Eastern Europe

Opportunities for increased trade in Poland and Czechoslovakia are being explored by Fisons Chemicals (Export) Ltd. One of their salesmen, Mr. D. A. Diamond, has been in Poland at the Poznan Fair. In Warsaw he visited the Foreign State Trading Organisation, CIECH, and technical departments concerned with the chemical industry.

In Prague he had discussions with CHEMAPOL, Czechoslovakia's Foreign Trade Organisation for chemicals, and with technical experts from various plants.

Fison products include pesticides, pharmaceutical and industrial chemicals, medical and veterinary preparations, and laboratory glassware and apparatus.

Fertilisers are cheaper

For the third successive year Fisons have cut the price of agricultural fertilisers. On July 1 all compound fertilisers came down by an average of over £1 per ton. Fisons 41, the most widely used compound fertiliser, is reduced by 25s. per ton. Superphosphates now also cost less—triple superphosphate by as much as £2 7s. 6d. per ton.

During the July-April period of 1959-60 farmers used about 19% more nitrogen, about 15% more phosphate and about 13% more potash than during the same period of 1958-59.

Fisons are also putting into effect economies made possible by the introduction of a range of high-concentrate fertilisers incorporating ammonium nitrate produced at their new Thameside factory at Standford-le-Hope, Essex, which was opened last year.

More substantial rebates will be offered as early delivery incentives and these, combined with the lower prices, will save farmers nearly £1½m. in 1960-61. This brings the total savings effected by Fisons price reductions over the past three years to more than £3m.

How much less will farmers be paying than they were before the first price reductions were made in 1958-59? On compound fertilisers the average savings over the past three years total £2 17s. 6d. per ton. The most popular compound fertiliser of all (Fisons 41) has come down in price by £3 2s. over the same period. In the previous two seasons price reductions averaged 15s. per ton and 20s. per ton respectively.

Hazards of photo-copying chemicals

Dr. J. C. Graham, of Highgate, an industrial medical officer, in a letter to *The Lancet*, says a recent article in a business management journal, describing a process in photocopying, mentioned trichlorethylene and tricresylphosphate without giving warning of their properties. "Trichlorethylene is not only an anaesthetic but has been described as producing mental changes due to prolonged absorption, and is a drug of addiction."

"Tricresylphosphate is not only equally toxic but is also a cumulative poison attacking the nervous system and, what is more important, it is absorbed through the skin."

He was also told that an alternative method was to use a mixture of equal parts of carbon tetrachloride and castor oil. "This seems an equally suspect process in view of the anaesthetic effect of carbon tetrachloride, and the same chronic effect on the kidneys and liver."

Dr. Graham says much of the work is probably carried out in the least suitable places—an ill-ventilated basement, for example.

£4m. acetic acid plant will use new process

The Distillers Company is to construct a new acetic acid plant at Hull, costing some £2m. This plant will be the first of its kind in Europe. It will use a new pro-

cess developed by the D.C.L. research department at Epsom and based on the direct oxidation of a light petroleum fraction. It is expected that the plant will be in operation early in 1962, when a proportion of the company's output of acetic acid will be made by this new process.

The Company has had a long experience in the manufacture of acetic acid, which is produced by a two-stage process from ethyl alcohol. The alcohol is first dehydrogenated to acetaldehyde, which in turn is oxidised to acetic acid. Until 1951, the ethyl alcohol was obtained by the fermentation of molasses. In that year, ethanol synthesised from ethylene became available from the petrochemical plant at Grangemouth, jointly owned by D.C.L. and B.P.

Howards' new plants

During 1959 the main plant expansions undertaken by Howards at Ilford were the construction of a phthalic anhydride plant and the rebuilding of the recrystallisation stage of the aspirin plant. The major projects for 1960, all of which are now well advanced, are the rebuilding of the remaining section of the aspirin unit, the rebuilding on a considerably increased scale of the unit producing cyclic ketones, mainly cyclohexanone and methylcyclohexanone (*Sextone* and *Sextone B*), and a substantial extension to the production facilities for sorbitol 70% syrup. All three projects should be completed before the end of February 1961.

Howards are the major manufacturers of cyclic ketones and the only manufacturers of sorbitol in the U.K. When the plant extensions for these products are completed there will be, in each case, considerable excess capacity.

Alkyl phenol ethoxylates from Marchon

Large-scale manufacture of alkyl phenol ethoxylates has now been started by Marchon Products. These non-ionic surfactants will cover two main series, the octyl phenol ethoxylates and the nonyl phenol ethoxylates, and will be marketed under the trade mark *Empilan*.

In addition, a range of sulphated alkyl phenol ethoxylates are being developed and information on these will be available from Marchon shortly.

£50,000 for new university

Pfizer Ltd. will subscribe £50,000 towards the establishment of a Kent University.

Mr. P. V. Colebrook, managing director of Pfizer, said: "The sponsoring body believe it possible to establish the University within the present decade—but this will only be practical if they receive enough financial support. In making this first contribution from a Kent industry we hope that our example will be followed by others."

Tax lifted from more drugs and medicines

A new Treasury order (S.I. 968) extends the schedule of essential drugs and medicines exempt from Purchase Tax.

New items exempt from tax and extensions of existing items (*italics*) are as follows:

HEAD I

Any one of the following substances, prepared for use by injection:

Aqueous solutions of amino acids with vitamins and mineral salts, whether with or without one or more of the following substances, that is to say, sorbitol, casein hydrolysate, glucose and ethanol;

HEAD II

Aluminium glycinate, whether or not mixed with either or both of the following substances, that is to say, magnesium carbonate and magnesium trisilicate;

4-tert-Butyl-2-chlorophenyl methyl methylphosphoramidate;

2-*o*-Chlorobenzyl-thio-4-dimethylamino-5-methylpyrimidine hydrochloride; Chlorthoroxazin mixed with phenacetin; Cyclophosphamide;

Dequalinium Salts, 1-alkyl-4-aminoquin-aldinium salts, and mixtures of these substances;

3:3'-Diamidinocarbaniide, and salts thereof;

2:4-Dichlorobenzyl alcohol with amyl-m-cresol;

1-*p*-Hydroxyphenyl-2-(1-methyl-2-phenoxy-ethylamino) propan-1-ol hydrochloride;

Inproquone, and the 3:6-dimethoxy-ethoxy analogue;

Metformin;

Quaternary cationic detergents, with bactericidal activity, and mixtures of two or more of such substances;

2,3,5-Tri-(1-aziridinyl)-1:4-benzoquinone;

HEAD III

Diethylaminoethyltheophylline camphor-sulphonate;

alpha-Ethyl-*alpha*-methyl-succinimide;

P.A.T.A.

The 1960/61 edition of the P.A.T.A. Year Book, just published, contains a comprehensive list, arranged in alphabetical order, of the products of the manufacturer members of the Association. Against each article listed is an indication of the relevant purchase tax rate (if any). Prices of the articles listed are not quoted because in previous editions, owing to alterations in purchase tax, they became out of date shortly after publication, thus rendering the list an inaccurate guide to current prices. It should be noted, however, that prices of additions to the P.A.T.A. and current price revisions will continue to be quoted in the P.A.T.A. Quarterly Record.

Furazolidone, and its 5-morpholinomethyl derivative;

Guanethidine sulphate;

N-Methyl-5-methylazadecylamine methobromide, in a polymerised form;

Pentaerythritol tetranitrate, whether or not mixed with glyceryl trinitrate;

Phenazocine, and salts thereof;

Piperazine adipate and piperazine citrate;

Piperazine, and salts thereof, prepared for anthelmintic use;

(Transferred from Head II)

Sennosides A and B, and salts thereof; preparations of senna fruit standardised in terms of sennosides A and B;

Sulphinpyrazone;

Thioridazine, and salts thereof;

Any antimicrobial substance being:

(a) a substance synthesised by bacteria, fungi or protozoa; or

(b) a substance the chemical properties of which are identical with, or similar to, any substance within paragraph (a) above; or

(c) a salt or derivatives or a salt of a derivative of any substance within paragraphs (a) and (b) above; or (d) any substance within paragraph (a), (b) or (c) above mixed with one or more of the following substances, that is to say, *NN'*-di-(4-amino-2-methyl-6-quinolyl) urea hydrochloride, kaolin, parahydroxybenzoic esters, quaternary ammonium bactericides and salicyl alcohol.

HEAD IV

Vaccines prepared from attenuated strains of poliomyelitis virus.

All vaccines have now been re-grouped under this Head.

All drugs and medicines previously exempt under the revoked Orders remain exempt under the new Order, but certain of the drugs now appear under the name approved by the British Pharmacopoeia Commission.

Copies of the Order are obtainable (price 6d. net., by post 8d.) from H.M. Stationery Office, York House, Kingsway, London, W.C.2, and branches or through any bookseller.

The Year Book, which is distributed to all members of the P.A.T.A. (including 11,500 chemist retailers), constitutes a useful and convenient work of reference. Price to non-members 2s. from P.A.T.A., 43 Gordon Square, London, W.C.1.

Darenthin tablets

Burroughs Wellcome and Co. are now issuing, in addition to the original 200 mg. scored tablet, a 50 mg. tablet of Darenthin (bretylum tosylate), the new hypotensive drug which acts by selective sympathetic blockade.

It is recommended that the initial dose of Darenthin should be small, since some patients may be maintained on a very low dosage.

Surface activity group membership over 200

The annual dinner of the Surface Activity Group of the Society of Chemical Industry was held in London on Monday, April 25, when the guest of honour was Sir Harry Melville, F.R.S., Secretary, Department of Scientific and Industrial Research.

The A.G.M. was held prior to the dinner, when a membership of 205 was announced. The Officers and Group Committee appointed to serve for 1960-61 are:

Chairman: Sir Eric Rideal, F.R.S.

Hon. Treasurer: R. C. Tarring.

Hon. Recorder: F. Riley.

Hon. Secretary: M. K. Schwitzer.

Membership and other details can be obtained from either the Hon. Secretary, Mr. M. K. Schwitzer, Armour Hess Chemicals Ltd., 4 Chiswell Street, London, E.C.1, or the Hon. Recorder, Mr. F. Riley, Marchon Products, 140 Park Lane, London, W.1.

Wellcome grant to U.S.

The Wellcome Trustees have made a grant of £50,000 (approximately \$140,000) to the Massachusetts General Hospital, Boston, for the establishment of a Henry S. Wellcome Research Chair in Medical Science. This is the largest single grant to be made by the Wellcome Trustees to a medical research centre in the United States.

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(Continued from page 304)

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People

New chairman and managing director for Boots

Mr. J. P. Savage, chairman and managing director of Boots Pure Drug Co. Ltd., will retire on March 31, 1961, by which time he will be 65. He will be succeeded by Mr. Willoughby R. Norman as chairman and head of the company and by Mr. F. A. Cockfield as managing director and chairman of the executive management committee. Mr. K. D. Williamson will become deputy managing director.

Mr. Savage is only the third to hold the office of chairman and managing director since the foundation of Boots Pure Drug Co. Ltd. in 1888. His predecessors were Jesse Boot (first Baron Trent) and his son, the second Lord Trent. The chairman-designate has been vice-chairman of Boots since 1954. He was born on October 12, 1909. In 1934 he married the Hon. Barbara Jaqueline, eldest daughter of the late Lord Trent. They have one son and two daughters. He joined Boots in 1945, after serving with the Grenadier Guards during the war.

In 1951 he was appointed to the board and became assistant general manager working directly under Mr. Savage. He was appointed vice-chairman when Mr. Savage took over as chairman in 1954.

Mr. Cockfield, who will become managing director, has been finance director since 1953. He was born on September 28, 1916, and was educated at the London School of Economics. He joined the Inland Revenue in 1938. In 1945 he succeeded Mr. S. P. Chambers, now chairman of I.C.I., as director of statistics and intelligence. He joined Boots in 1952 as a member of the executive management committee. In 1955 he became a director of all the subsidiary companies. He was married in 1943 and has a daughter aged 16 and a son aged 12.

Mr. Williamson, who will become deputy managing director, has been on the board since 1959. He was born at Cambridge on June 9, 1909. He was educated at King Edward VI's School, Norwich, and Trinity College, Cambridge, where he studied law and was later called to the Bar at the Middle Temple. He joined Boots in 1930. He was married in 1932 and has one son.

Fertiliser Society

Dr. H. L. Richardson has been elected president and Dr. G. W. Cooke, vice-president, of the Fertiliser Society.

J. H. Hudson, A. H. Kaye and J. H. H. Peak have been elected to fill vacancies on Council.

Pharmaceutical Society officers

The officers of the Pharmaceutical Society for the coming year are: Presi-



J. P. Savage



W. R. Norman



F. A. Cockfield



L. N. Borra

dent, Mr. Thomas Reid, "June Meadow," Haslemere; vice-President, Mr. H. S. Grainger, chief pharmacist, Westminster Hospital; treasurer, Mr. W. Spencer Howells, "Springfield," Spring Gardens, Whitland, Carmarthenshire.

A. E. Honeyman, managing director, the Mentholatum Co. Ltd., last month visited the parent company in Buffalo, New York, to discuss marketing and development plans.

A. D. Wilson, whose father, A. L. Wilson, is chairman of John and E. Sturge Ltd. the Birmingham chemical manufacturers, has joined the board. He will continue to be general manager of the company's works at Selby, Yorks, which is concerned mainly with the production of citric acid by the industrial mould fermentation process.

D. A. Hampshire, assistant managing director, F. W. Hampshire and Co. Ltd., and **R. Beckett**, the advertising director, have been studying new product trends in Canada and the U.S.

R. Shirvell Price, formerly public relations manager, has been promoted to the new position of group organisation manager, Bayer Products Ltd. and Winthrop Products Ltd.

Other appointments in the group are: **A. P. Dickson** (marketing controller), **Dr. K. Boheimer** (medical controller), **G. T. Smith** (commercial controller) and **F. W. Whiting** (development controller).

J. F. Perkins, a member of the Pyrethrum Board of Kenya since 1956, has been elected vice-chairman. Mr. Perkins, who farms near Kitale, was formerly general manager of the Magadi Soda Co., Kenya (an I.C.I. subsidiary). He replaces **R. T. Mytton Watson** who resigned in March.

Livio N. Borra has been made a director of T. Giusti and Son Ltd., stainless steel equipment fabricators. London born Mr. Borra, who first joined Giusti 18 years ago, has been closely connected with the firm's expansion from ice cream, dairy and food equipment into petroleum and chemical processing.

Bernard F. Howard, J.P., F.R.I.C. has resigned from the board of Howards and Sons Ltd., and has been elected President of the company. He is 80, and has been a director for 57 years.

C. W. Robinson, pharmaceutical development director of Evans Medical Ltd., has been appointed president of the Liverpool Chemists' Association for 1960/61.

Thawpitt Ltd. announce the appointment of **Edward Alfandary** as managing director. **Captain T. E. Thorpe**, formerly chairman and managing director, remains chairman.

Dr. A. Michaelis, editor of *Discovery*, will be joining Ciba as director of information on August 1. He will assume world-wide responsibility for Ciba's scientific public relations.

Burroughs Wellcome and Co. have appointed **H. B. Lomas** assistant sales director. He will be responsible for the home, overseas and veterinary divisions.

H. A. Cocking, manager of the home sales department (medical), has been appointed general sales manager (veterinary division) in succession to Mr. Lomas.

The Aluminium Development Association has appointed **Gen. Sir Geoffrey Bourne**, Director-General, to succeed **Air Commodore W. Helmore**, who recently retired after 14 years in the post.

International Flavors and Fragrances have appointed **Henry van Ameringen** as perfumery sales manager of their branch, Polak and Schwarz (England) Ltd. He has worked in the company's sales departments in Holland, France and the U.S.

Shell Chemical Co. Ltd. announce that **L. G. J. Engle**, manager of their southern sales region, has retired.

M. B. Creed, who is appointed his successor, joined the Shell Group in 1938 and after war service transferred to the chemical side of the Group.

New plants help Laporte to increase profits by 73%

The Laporte Group are now reaping the reward of years of capital expenditure and product development. Last year (to March 31) their profits before tax rose to £3,147,943, 73.6% higher than the previous year and the best in the company's history.

These fine results came in the first year of office of the new chairman, Mr. P. D. O'Brien. In spite of the good profits dividend is being kept to a modest 12% compared with 8% the year before. Assets of the Group now stand at £5,471,001.

Dealing with the various subsidiary companies of the Group, the annual report states that Laporte Chemicals Ltd. "has consolidated its position as a manufacturer and world supplier of hydrogen peroxide. . . . Although world production has risen substantially, it would appear that consumption is more than keeping pace with it."

Other developments in connection with this company are the "increasingly important part" played by the manufacture of organic peroxide products; the completion of a sodium chlorite plant; and the completion of new £48,000 laboratories at Warrington.

During the year Laporte Titanium Ltd. emerged from the stage of meeting heavier depreciation charges on fixed assets not fully employed.

Plants were for the most part working

at full capacity, and the board has embarked on a further phase of development at Battery Works, Stallingborough, which it is estimated will cost £3.5 million and will increase the output from 30,000 tons per annum to 50,000 tons p.a.

The widening of the company's interests by manufacturing titanium nickel yellow, the introduction of a range of special products for the ceramic industries, and developments in the field of organic titanium compounds are also mentioned.

Laporte Acids Ltd. has had a successful year's trading and is engaged in integrating the various sites and widening the scope of its business.

The results of the Group have also benefited by the acquisition of three additional companies which are described as "The Sheffield Group"—Glebe Mines Ltd. and James Wilkinson and Son Ltd., whose acquisition "has enabled the company to enter the field of fluorine chemistry, with a consequent broadening of the base of our business"—and the Sheffield Chemical Co. Ltd.

The Fullers Earth Union has had a successful year. In particular, comment is made that "the high level of output in the foundry industry as a result of increased activity in the motor industry, has resulted in an excellent demand for the company's *Fulbond* foundry bonding materials."

"The Raw Materials of Progress"

In conjunction with their annual report 1959/60, Laporte Industries Ltd. have produced a full colour book—"The Raw Materials of Progress."

The book is being issued simultaneously to shareholders and to the Group's major customers, and—in the form of a special number of the Laporte House Magazine—to the company's 4,000 employees.

The book outlines the company's work and its history. It is split into three sections—"The Group"; "The Raw Materials of Progress"; and "The Future."

The first part tells of the growth of the Group, from the hydrogen peroxide works which Bernard Laporte established at Shipley in the '80s, to be one of the largest organisations in the British chemical industry.

Today the Group consists of 11 companies, employing 4,000 people operating 16 production units in this country, Australia and Canada.

The amount of specialised plant and equipment in which the Group has invested is steadily increasing and in total it represents some £12 million, out of a total capital of £20 million. In recent years Laporte have been investing in new plant at the rate of £1,500,000 a year.

Laporte products, says the book, are "unseen but essential components of hundreds of everyday objects. . . . They are the stuff of experiments which offer still greater prospects for tomorrow. They are the raw materials of progress." And Part Two of the book deals with the various products of the Laporte companies: peroxide as a chemical and fuel, sulphuric acid, titanium oxide and fullers earth.

In addition to these major products Laporte also manufactures many other chemicals—the Luton plant alone makes over 100 different products in 19 different categories. Others require unusual and specialised manufacturing processes—Laporte fluorine compounds, for instance, may be said really to begin their lives in the Group's own fluorspar mines at Eyam.

The final part of the book deals with "The Future—Where is Laporte going?" The search for new products, research into new processes and techniques, training for automation, manufacturing technology, overseas expansion, management and men, money and materials—all these and many more provide the intangible raw materials of the technical progress of tomorrow.

"It is through them and what they will produce," the book concludes, "that Laporte will make its continuing contribution to industrial prosperity and the future. . . ."

Engineers move

Rhodes, Brydon and Youatt Ltd. have moved their head office to Reddish Engineering Works, Stockport, Cheshire (Heaton Moor 6211).

Two Meldola medallists

The Meldola Medal, which is the gift of the Society of Maccabæans, is normally awarded annually, the award for a particular year being made to the chemist who, being British and under 30 years of age at December 31 in that year, shows the most promise as indicated by his or her published work. Awards are made by the Council of the Royal Institute of Chemistry, with the concurrence of the Society of Maccabæans.

Since the Medal was first instituted in 1921 awards have been made every year, except for the war years 1942-45, inclusive, when they were suspended, and for 1934 and 1958, when it was concluded that no candidate had produced evidence of original work of the exceptional quality required. On the other hand, two awards were made for each of the years 1936, 1946, 1951 and 1952, when there were two candidates adjudged to be of equal merit in diverse fields of work. For the same reason it has been decided to make two awards of the Meldola Medal for 1959. The recipients will be:

John Ivan George Cadogan, for his work in the field of organic chemistry, with special reference to reactions of free radicals in solution and to reactions of organophosphorus compounds. He is a lecturer at King's College, London.

Thomas Cudworth Waddington, for

his work in the fields of physical and inorganic chemistry, with special reference to thermochemistry and reactivity of azides; photoconductivity of anthracene; lattice energies and infra-red spectra of inorganic salts; and liquid hydrogen chloride as an ionizing solvent. He is a university demonstrator in chemistry at Cambridge.

£1½m. chlorine plant

Plans to increase chlorine production by 50% at its Elworth, Cheshire, works are announced by Murgatroyd's Salt and Chemical Co. Ltd, the jointly-owned subsidiary of Fisons Ltd. and The Distillers Co. Ltd. The new plant will cost about £1½ million, and is scheduled to come into production in the latter half of 1961. Project managers for the expansion are the D.C.L. Engineering Division, and main contractors for the plant construction and installation are W. J. Fraser and Co. Ltd.

Through D.C.L., Murgatroyd's is associated with British Hydrocarbon Chemicals Ltd., whose current programme of expansion at Grangemouth, Stirlingshire, includes a new ethylene dichloride plant, and with British Geon Ltd., who recently announced a scheme for increased production of polyvinyl chloride at Barry, Glamorgan.

Topics for Pharmaceutical Conference

The address of the chairman, Prof. W. H. Linnell, at the opening session of the British Pharmaceutical Conference, Newcastle upon Tyne, on Monday morning, September 5, will be entitled "Academic Research and the Five Freedoms."

The subject for the Symposium Session on Thursday, September 8, will be "Chemical Disinfection" and the discussion will be opened by S. E. Jacobs, J. G. Davis, A. H. Walters, and A. M. Cook.

The subject for the Professional Session on Tuesday, September 6, will be "Change to the Metric System in Pharmaceutical Practice" and the discussion will be opened by K. R. Capper.

The subject for the Professional Session on Friday, September 9, will be "Professional Responsibilities of the Pharmacist in the Supply of Medicinal Substances" and the discussion will be opened by C. G. Drummond, Prof. A. D. Macdonald and H. Noble.

Chlorothiazide patents

U.K. Patents 826921, 826922, 826923 and 826924 have now been granted to Merck and Co. Inc. of Rahway, New Jersey, covering certain benzothiadiazine derivatives, including chlorothiazide, and processes for their preparation. Merck Sharp and Dohme Ltd. of Hoddesdon, Herts., have been made exclusively responsible by the patentees for the manufacture, tableting, distribution and sale of such derivatives throughout Great Britain, and any other manufacture, distribution or sale is unauthorised.

New carbide plant in Ulster

Carbide Industries Ltd., one of the British Oxygen group of companies, has opened a plant at Londonderry, Northern Ireland. It will initially produce about 50,000 tons p.a. of calcium carbide which will be converted into acetylene in continuous generators. The entire output is pumped by pipeline to the nearby Du Pont factory where it is used for the manufacture of neoprene.

The basic materials, coke and limestone, are imported by sea and are unloaded at a special wharf.

The site comprises 60 acres of which 25 acres have been developed.

Three hundred people are employed in the new plant. The managing director of Carbide Industries is Dr. R. F. Goldstein.

Drug economy probe

The Central Health Services Council has, at the suggestion of the Minister of Health, appointed a Standing Committee, under the chairmanship of Lord Cohen of Birkenhead, to advise on operational research in the pharmaceutical services.

Boots profits increase by 51%

A remarkable 51% rise in profits in the last year was achieved by Boots Pure Drug Co. Ltd. On a turnover of £90.5 million profits before tax amounted to £7.5 million against just under £5 million last year.

Mr. J. P. Savage, chairman, said that the profits rise was due to a sales increase of £6.75 million without any increase in staff.

Manufacturing had made an important contribution to profits, partly by increased output and partly by improved efficiency.

Another contribution was made by the employment of better warehouses and equipment at all main depots. Method study and other techniques were being used to still further increase efficiency. "Dramatic changes" in

warehouse equipment and assembly methods could be expected from current projects.

The pattern of overseas trading had changed. Sales of bulk chemicals had declined because of intense competition, but losses had been made good by increased sales of branded products, particularly those resulting from Boots' own research. Sales of overseas companies, all in the Commonwealth, rose by 15% to over £2.5 million.

"Although we are budgeting for increased profits this year," says Mr. Savage in his annual statement, "I must warn shareholders that it is on a much more modest scale than for last year, when the figures were affected by the complete replanning of a number of our activities."

The Committee's members include general practitioners, business men, an economist and a statistician.

Its terms of reference are:

"Having regard to the need to avoid unnecessary expenditure in the pharmaceutical services provided under Part IV of the National Health Service Act, 1946, to advise the Minister on (1) the operational research which should be undertaken in relation to those services, involving the collection of statistical, economic and socio-medical data, and on (2) the interpretation of such data."

Cattle drug sent to Germany

In response to an urgent request from North Germany, where an acute epidemic of parasitic bronchitis (husk) has broken out among cattle, the Wellcome Foundation Ltd. has sent supplies of the drug *Franocide* to Hamburg by air and sea.

Husk, an inflammation of the lung caused by a parasitic worm, is endemic in cattle in the United Kingdom, where it causes losses estimated at between £2 or 3 million annually.

It speaks well for British chemists that German agriculture should turn to Great Britain for the remedy.

Penicillin expert becomes Wolfson research professor

Dr. Dorothy Hodgkin, F.R.S., university reader in X-ray crystallography, and fellow of Somerville College, Oxford, has been appointed by the Royal Society as the first holder of the Wolfson Research Professorship.

Dr. Hodgkin, who will take up the appointment on October 1, 1960, will continue her investigations at Oxford of the structure of complex organic molecules by the method of X-ray crystal analysis. Her best known work is perhaps that on the structure of penicillin and more recently on the complete elucidation of the structure of vitamin B₁₂, in

which she showed that it was possible to apply the methods of X-ray analysis to elucidate structures of molecules which are too complex to yield to the ordinary methods of chemistry.

The offer of the Isaac Wolfson Foundation to create a special fund of £200,000 for the endowment of a Wolfson Research Professorship of the Royal Society was made a few months ago.

Cosmetic chemists elect new president

At the Twelfth a.g.m. of the Society of Cosmetic Chemists of Great Britain the president, Dr. R. H. Marriott, delivered his report of Council for the year. He mentioned that membership had increased by 18 to 323. A successful Congress had been held at which 268 had paid the fee for participation.

During the year a milestone had been the successful founding of the International Federation of Societies of Cosmetic Chemists. Belgium, Denmark, France, Germany, Great Britain, Norway, Sweden and U.S.A. participated. Mr. M. G. de Navarre had been elected President of the Federation and its work is being carried out by a Committee consisting of the President, Dr. Masch and Dr. Marriott.

The following new officers of the Society were returned unopposed:

President: H. W. Hibbott, M.Sc., Ph.D.
Hon. Sec: L. S. Smith
Hon. Treas: M. P. Bailey

The election of three persons as Members of Council from four candidates resulted in the following being returned:

D. F. Anstead, B.Sc., A.R.I.C.
R. Clark, A.R.I.C.
R. F. L. Thomas, B.Sc., A.R.C.S.

The new President then took the chair. His first task was to present Dr. Marriott with a scroll commemorating the honorary membership which the Society had conferred upon him.

Dunlop Chemical Products Division

Dunlop's compositions division has been re-named Dunlop Chemical Products Division. The General manager of the division is Mr. N. G. Bassett Smith, this year's chairman of the British Rubber and Resin Adhesive Manufacturers' Association. Last month, Mr. Smith, accompanied by Mr. T. Thomas, the division's technical manager, left for a month's tour of prominent American chemical plants.

A wide range of products are now being made at the division's factory in Birmingham, among which, adhesives, based not only on natural rubber but also on reclaimed rubber and synthetics of all kinds, are a major item. Last year 1,500,000 gal. went to the motor industry alone.

Pressure gauge standard

British Standard for Bourdon tube pressure and vacuum gauges (B.S.1780:1960). Prepared by a committee of experts, this new publication (60 pp., 18 illustrations) specifies requirements for indicating pressure gauges, vacuum gauges and combined pressure and vacuum gauges of the bourdon tube type. The range of nominal sizes is 2-12 in.: and the maximum scale readings are up to 16,000 lb./sq. in. or up to 6 tons/sq. in.

Copies may be obtained from the British Standards Institution, 2 Park Street, London, W.1, 15s. net.

Control laboratory design

The services of the laboratory engineering department of C.J.B. Automatic Control Division are now available to all industries. The Department has gained extensive experience over a wide field in designing and installing process laboratories on CJB projects. This experience, supported by the Automatic Control Division, enables the department to offer a service of complete responsibility, from initial consultancy to final commissioning, of any laboratory in any industry.

Sir C. Dodds heads farm chemicals committee

The Minister of Agriculture has appointed Sir Charles Dodds, F.R.S., to be chairman of the interdepartmental advisory committee on poisonous substances used in agriculture and food storage. Sir Charles, who succeeds Sir Solly Zuckerman as chairman of this committee, is Courtauld Professor of Biochemistry in the University of London. He has served since 1951 as the chairman of the Preservatives Subcommittee of the Food Standards Committee.

The Committee was appointed in March 1954 to keep under review all risks that may arise from the use of toxic substances on agricultural products and in the storage of food, and to make recommendations to the Ministers concerned.

Technical Press Review—July

Automation Progress.—Information Searching by Computer; The British Computer Industry Today; Optical Digitisers Today; Standardisation of Data Processing Ancillaries; How to Study the Feasibility of Buying a Computer; Mechanical Handling Today; Synchros—How they work and who makes them; Automation on the Railways—4; Automatic Inspection Devices; Modern Digitising Techniques; A New Computer Storage Device.

Chemical and Process Engineering.—Solvent Recovery: Adsorption and its application to solvent recovery; The design of a continuous counter-current adsorber; Some new designs in solvent recovery plant; Materials of Construction for Chemical Plant—Nickel; Chemistry and Ceramic Nuclear Fuels; Chemical Engineering Fundamentals—2; Developments in Wood Distillation.

Dairy Engineering.—Milk Cartoning is Big Business in the States; Mechanical Handling Paves the Way for a Five-day Working Week; Colombia's Contribution to Dairying in South America; Milk Cartoning by Tetra Pak in Germany; Practical Cleaning Routines for the Dairy—6.

Food Manufacture.—Factory articles: John Rannoch Ltd., The Richmond Sausage Co. Ltd.; World Food Supplies—6; Quick Freezing and Refrigeration.

Fibres and Plastics.—Fibres for Bonded Fabrics; Electronics in the Textile Industry; Progress in Antistatics for Textiles; Fibre Amalgamating Equipment; Wool/Dacron Processing in America; Analysis and Testing of Plastics; Formulating PVC for Chemical Plant; Dry Colouring Polypropylene.

Paint Manufacture.—Developments in paint making machinery; Equipment for the Manufacture of Emulsions; Polyester Resins in Wood Finishes—3; A Comparative Study of Polyvinyl Acetate, Copolymers and Acrylics in Emulsion Paints; Advanced Paint Chemistry—II.

Petroleum.—In-Line Blending at Ellesmere Port; New Developments in Oil Hose; British Engines and Generators for Indian Pipelines; Pipelines Come to Europe; The Second Saharan Pipeline; Pipeline Developments and New Techniques; Oilfield Development—7.

World Crops.—Timber for Agricultural Buildings; Imperata Cylindrica; Herbicides in Sisal Cultivation.

For specimen copies and subscription forms apply to the Circulation Manager, Leonard Hill House, Eden Street, London, N.W.1.

Fires cost £40m.

"A national disgrace" were the words used by Mr. A. F. O'Shea, chairman of the Fire Protection Association, to describe the country's bill for fire losses in 1959. In his statement accompanying the annual report of the Association Mr. O'Shea draws immediate attention to this £44 million blow struck to the national economy last year. He said the public should be horrified by the alarming increase in very large fires, some costing over £1 million, and he emphasised the need for more awareness of fire hazards and for continuing protective measures.

The 1959 Factories Act, said Mr. O'Shea, would give the Government increased power to enforce more fire protection in industry.

Flammable liquids: a warning

Every year a large number of people are killed or injured, and much damage done to plant and property by fires and explosions arising from the use of flammable liquids.

An outline of the precautions to be taken to reduce the risks of such accidents, which exist whether the quantities used are large or small, is given in an advisory leaflet which has been sent to every factory owner or occupier recently by Mr. T. W. McCullough, Chief Inspector of Factories.

The leaflet draws attention to the need for some knowledge of the properties of the liquids used in the factory, and what the risks are. It suggests the substitution of less dangerous liquids for those in use where this is technically possible.

Measures to prevent accidents which it describes include restriction of the spread of any spillage of flammable liquids, the removal of vapours by ventilation, cleaning of empty vessels, the safe distribution of liquids, and the elimination, as far as possible of all sources of ignition from rooms or other enclosed spaces where there are flammable liquids.

Warnings are given about the importance of design of protective clothing which could be removed quickly and easily in an emergency, and of the need to prohibit the washing of hands or overalls in flammable liquids.

Increased polymer capacity

Proposals are being considered by Imperial Chemical Industries Ltd. to extend the existing capacity for vinyl chloride polymers at their Hillhouse works in Lancashire by 10,000 tons, the extension to be in operation by the middle of 1961. Their present capacity for polymer manufacture is about 70,000 tons compared with 55,000 tons in 1958. The increase to the present 70,000 tons has been achieved by the application of new manufacturing techniques on the existing plants. It is proposed to make an extension in p.v.c. compounding capacity in parallel with the polymer extension.

Drug control urged

One hundred and sixty representatives of branches of the Pharmaceutical Society in England, Scotland and Wales decided, at their annual meeting in London, that the society should press for legislation to ensure that no new substance introduced for medical treatment should be supplied to the public, except on a doctor's prescription, until sufficient evidence is available to justify release from such control.

Flu eradication

Eradication of poliomyelitis as a practical possibility was foreshadowed by V. M. Zhdanov, academic secretary, Academy of Medical Sciences of the U.S.S.R., at the Thirteenth World Health Assembly in Geneva. He was not so optimistic about influenza, which, he said, was "the only truly world-wide infection." Large-scale vaccination was not the answer, as it may prove to be in the case of polio. The influenza problem would not be solved until other methods of control were discovered, such as special types of antibiotics, he said.

Dr. Whittet honoured

At a ceremony held in conjunction with the annual meeting of the Guild of Public Pharmacists in London, Mr. J. Smith, a director of Evans Medical Ltd., presented an Evans Medal for merit in pharmacy to Dr. T. D. Whittet, who is on the staff of the University College Hospital and Medical School as chief pharmacist and lecturer in pharmacy.

In presenting the medal Mr. Smith said that in hospital pharmacy there was a full share of public service but probably not an equal share of public acclaim. Evans Medical hoped that this presentation would help to add to the public recognition of a distinguished pharmacist.

S.C.C. equip beauty room at hospital

Cosmetics and hospital treatment were linked when a new beauty room was opened at Halliwick Hospital, New Southgate, London. The equipment was provided by the Society of Cosmetic Chemists of Great Britain. The opening ceremony was performed by Dr. R. H. Marriott, President of the Society, in the presence of the vice-chairman of the East Barnet Hospital Management Committee.

In his opening speech Dr. Marriott briefly gave the background to the donation. Miss Eleanor Macdonald, then of Atkinsons Ltd. had given an account to the Society of the beneficial effects of beauty treatment on mental patients in hospitals. Following upon this, Mr. Polan, a Council Member of the Society, had proposed that the Society provide the equipment for a beauty room at a mental hospital and this had now been done. Dr. Marriott hoped that the notion would now be adopted by other hospitals.

Laporte to buy Spence

Laporte Industries Ltd. have made an offer for the 5% cumulative preference shares and the ordinary shares of the old-established family business of Peter Spence and Sons Ltd., for a total cash consideration amounting to approximately £2,500,000.

This offer was made in agreement with Mr. Derek Spence and his co-directors of Peter Spence and Sons Ltd. who have recommended it to their shareholders. Acceptance by a majority of shareholders has been assured.

Peter Spence is engaged at Widnes in the manufacture of a wide range of heavy chemicals including aluminium sulphate, sulphuric acid, catalysts and organic titanium compounds. The business is, in certain respects, complementary to the existing interests of the Laporte Group.

Pfizer buy more land

Pfizer Ltd. have purchased the Richborough Port, Sandwich, Kent.

The area of land involved—which adjoins the present 80-acre site of Pfizer Ltd.—is approximately 89 acres and it has a frontage of about one mile.

Mr. P. V. Colebrook, managing director of Pfizer, said that the land will be used for the company's future development of chemical, pharmaceutical and agricultural products.

Sturge offer 600,000 shares, get applications for 14m.

When the old established fine chemicals firm of John and E. Sturge Ltd. offered 600,000 5s. shares at 11s. each last month they received no fewer than 14,738 applications for a total of well over 14 million shares. All applications by the company's employees (50,200) were met in full. The rest were rationed out by ballot. Thousands of unsuccessful applicants had their money returned. The offer was one of the most successful in recent Stock Exchange experience.

International fertiliser programme

A meeting of representatives of the fertiliser industry has asked the Food and Agriculture Organisation to invite the industry to contribute \$1 million over two years for an international fertiliser programme under FAO's Freedom-from-Hunger Campaign.

The objectives of the programme are: to promote the efficient use of fertilisers in order to increase food supplies in deficit areas and food supplies for animal production; to help governments develop national programmes of fertiliser use and production; to assist in selecting methods of spreading information on fertiliser needs and use, and to develop guidelines regarding fertilisers in foreign aid.

Work in the field, described as the most important part of the programme, would include fertiliser tests on cultivators' fields and extensive demonstrations of fertilisers. It would also involve deve-

lopment of soil-testing laboratories and services, and their use as a guide to better fertiliser and management practices.

The representatives approved in principle the aims, organisation and scope suggested for the programme, and agreed to recommend to their associations, companies and the industry that it deserved further examination and support.

Organotin compounds research

Prof. van der Kerk, Director of the Dutch Government's Institute of Organic Chemistry, and Professor of Chemistry at Utrecht University, recently visited the Nutrition Research Unit at Huntingdon, Leicester University and the Laboratories of the Tin Research Institute at Greenford.

Prof. van der Kerk has pioneered much of the research work on organotin compounds sponsored by the Tin Research Institute, and his visit to Huntingdon enabled him to confer with Prof. A. Worden on research work on the veterinary uses of organotin compounds.

At Leicester University Prof. van der Kerk, who was accompanied by Dr. E. S. Hedges, director of the Tin Research Institute, discussed with Dr. Eaborn, of the university's chemical department, progress in research into the chemical reactions of organotin compounds which is being undertaken at the University under the sponsorship of the Tin Research Institute.

Organotin compounds are being increasingly used as fungicides, insecticides, anti-rot agents in timber and fabrics, as an anti-slime agent in paper manufacture and as stabilisers in plastics.

Change of representation

There has been a change of representation for both Farrow and Jackson Ltd. and Purdy Machinery Co. Ltd. Mr. S. Holden has left the company and his territory has been taken over by Mr. I. Gordon of 47 Empress Avenue, Ilford, Essex.

The territory consists of the counties of Bedford, Cambridge, Derby, Huntingdon, Leicester, Norfolk, Northampton, Nottingham, Rutland, Stafford, Suffolk, Warwick and Worcester.

Packaging conference

Following the successful first packaging conference organised by the A.B.C.M. in March 1958, a second Conference will be held at the Hotel Majestic, Harrogate, from October 31-November 3. The Conference is limited to members of the Association and certain guests.

Container printing

Owing to the continued expansion of their screen printing division, Glastics Ltd. are now devoting the whole of their premises at 9 Salisbury Road, Barnet, Herts., to their printing works which is engaged in printing glass and plastics containers.

Mile-long effluent pipe

A mile of 18 in. dia. steel pipe was pulled into the Usk estuary recently to form the new pipeline for treated effluent from the Newport factory of Monsanto Chemicals Ltd.

The new line replaces a cast iron out-fall which was not large enough to handle the anticipated increase in the amount of treated effluent. The old line is now buried under the Usk Mouth power station coal dump and was not placed far enough out into the Bristol Channel.

Research award

The trustees of the Agnes Borrowman Trust, Professor J. W. Fairbairn and Sir Hugh Linstead, have selected Miss Isobel Beswick for the first award. She will continue her work in the School of Pharmacy of the Royal College of Science and Technology, Glasgow, under Professor J. P. Todd upon the bacterial lipopolysaccharides from an immunological viewpoint.

Protective gloves

The 17 types of glove specified in the revised British Standard for Industrial Protective Gloves (B.S. 1651:1960) offer protection against most industrial hazards to which the hands are vulnerable. Materials for the gloves fall into four groups: leather, plastics, rubber and cotton. Of the 17 types of glove specified in the 1950 edition, one has been discarded. It has been replaced by fabric-lined rubber gloves and gauntlets.

THE CHEMICAL MARKET

This Month's Changes

LONDON.—**Aspirin** in 56 lb. lots is down by 2d. to 5s. lb., 1 cwt. lots up 3d. to 4s. 11d. lb. and 5 cwt. lots down 1d. to 4s. 9d. lb. Changes in the **Iodides** include: Mercury red B.P.C. 12½ kg. lots down by 6d. to 58s. 6d. kg., Potassium B.P. 12½ kg. lots up by 1s. to 15s. 9d. kg., and Sodium B.P. 12½ kg. lots up 6d. to 22s. kg. **Nicotinamide** 1 kg. lots is up 1s. to £2 17s. 6d., and **Nicotinic acid** in both 12½ kg. and 1 kg. lots is down 1s. to 32s. 9d. kg. and 35s. kg. respectively.

Caustic soda, both solid in drums, dlvd., and flake 3½ cwt. lots is down £3 10s. to £34 6s. 6d. ton and £35 10s. 6d. ton respectively.

Phenol, ice crystals, under 1 ton dlvd. is down 1d. to 1s. 6d. lb. and over 10 tons is down 1½d. to 1s. 3d. lb.

Palm kernel oil, refined, deodorised, 2 ton lots is down £8 to £128 ton. **Palm oil**, refined, deodorised, 2 ton lots is also down by £1 to £100 ton. **Candelilla** Spot is down by 15s. to £24 5s. cwt. **Carnauba** Prime Spot is down by £1 5s. to £42 15s. cwt. **Tragacanth** No. 1 Spot and Pale Leaf are down £2 and £1 to £137 and £50 cwt. respectively.

New Products

Station early in 1955 and since that time it has been tested and developed extensively in field trials.

Manufacture of *Reglone* has now begun and it will be available in the United Kingdom for the 1960 haulm-spraying season.

Feed additive-tranquilliser

Serpasil a new tranquillising and blood pressure-lowering additive for poultry feeds, has been announced by Ciba Pharmaceutical Products Inc., U.S.A.

Specifically intended to boost productive performance in broilers and laying hens, and to control and prevent aortic rupture in turkeys, *Serpasil* is claimed to be the first feed additive of its kind.

Anti-coccidiosis drug

A new drug for combating coccidiosis, a poultry disease, was announced by Dr. R. S. Aries at the annual meeting of the Canadian Institute of Chemistry.

The new product—mepyrium—can be utilised either as a feed additive to prevent occurrence of coccidiosis or as a drug to cure the disease.

Dr. Aries' firm licenses commercial processes for synthesising mepyrium.

Tissue builder

Six and a half million elderly people in the U.S. suffering from geriatric malnutrition, a chronic underweight condition which is unresponsive to increased food intake and vitamin supplements, form the market for a new tissue-building drug called *Dianabol*.

Developed by Ciba Pharmaceutical Products Inc., *Dianabol* is taken orally in a dose of 1 to 2 tablets daily. An average daily dose of the drug should cost the patient about 17 cents.

Dyebath acid

Dispersol AFB is a new auxiliary product marketed by the Dyestuffs Division of I.C.I. to ensure level results when basic dyes are applied to acrylic fabrics such as *Courtelle*, *Acrlan* 16, *Orlon*, *Dralon*, etc. *Dispersol AFB*, which is in convenient liquid form, acts by restraining the initial rapid absorption of basic dye, allowing the temperature to be raised rapidly to the boil while at the same time promoting uniform uptake of dyestuff by the fibre.

Corticosteroid lotion

Merck Sharp and Dohme Ltd. have introduced *Decadron* skin lotion (Dexamethasone 21-phosphate). It allows a potent corticosteroid to be used in a wide variety of allergic and inflammatory skin conditions.

Decadron lotion is supplied in 15 ml. plastic squeeze bottles. Each ml. contains 1 mg. dexamethasone 21-phosphate (as disodium salt). List price 24s. Trade price 16s. Exempt Purchase Tax.



The new spray Pedrite for controlling footrot in sheep.

Spray controls footrot in sheep

An aerosol spray to control footrot in sheep has been developed by Boots.

Called *Pedrite*, it contains a bactericide and a colouring agent to indicate the exact area of the hoof covered.

Sprayed after the hooves of affected animals have been pared, *Pedrite* has been given extensive trials under all conditions on the company's farms. It is claimed that it is practically as efficient as antibiotics used against footrot, and is much cheaper in use.

One particular trial showed that untreated sheep lost an average of 5½ lb. in weight over a period of eight and a half weeks representing a total loss of 9s. 4d. a sheep. Treated animals, however, suffered no weight loss, and cost of treatment was 4d. a sheep.

The *Pedrite* aerosol spray cost 12s. 6d., and is sufficient to treat about 40 sheep.

Potato haulm destroyer

Reglone, a new, non-arsenical chemical which, it is claimed, destroys potato haulm without danger to human beings and livestock, will be available to farmers this season. As well as being safe to use, *Reglone* is said to be a more efficient haulm killer than the arsenical compound which it will replace.

This new chemical is the result of many years of work by I.C.I. Ltd. and Plant Protection Ltd. at Jealott's Hill and Fernhurst Research Stations to find a haulm destroyer which is as efficient as arsenic, does not harm human beings or livestock, leaves no harmful residue in the crop, and can be applied by farmers' own spraying machines. These four conditions are satisfied by *Reglone*, the active ingredient of which is diquat.

Diquat is new quaternary ammonium compound first prepared and patented by I.C.I. Its haulm-destroying qualities were discovered at Jealott's Hill Research

News from Abroad

AUSTRALIA

Aerosol propellants to be made

Consolidated Zinc Pty. Ltd. and Monsanto Chemicals Australia Ltd. have formed a jointly-owned company to manufacture chemicals in which they have common interests, especially in the fluorine field. The company will produce *Iscen* fluorocarbons which have for some years been made in the U.K. by Imperial Smelting Corporation, another member of the Consolidated Zinc group. These fluorocarbons, which are not at present made in Australia, are extensively used as refrigerants and pressure pack propellants. The plant, at Monsanto's site in Sydney, is expected to be in production by mid-1961.

KENYA

Record pyrethrum crop

Kenya plans a record pyrethrum crop for the coming year. Annual licences are being issued to farmers to permit a total production of about 10,300 tons of the flower. Previous highest production was 7,409 tons produced in 1945 under British Government wartime guarantee.

Forecasts suggest there is every possibility that the forthcoming year's production of pyrethrum will be fully absorbed. The value of these sales will be nearly £3½ million, as compared with pyrethrum exports to the value of £2,196,286 in 1959.

UNITED STATES

Varying action of hypotensives

Two new drugs reported to lower blood pressure without annoying side effects vary in their action when patients are standing up or lying down and appear to differ in their effect on systolic and diastolic blood pressures. This has emerged from reports by Dr. Louis A. Soloff of Temple University Medical Centre and Dr. Robert F. Maronde of the University of Southern California.

The physicians were addressing a conference on new diuretics and anti-hypertensive agents held by the New York Academy of Sciences recently.

The two drugs are bretylium tosylate (discovered in England by Burroughs Wellcome and guanethedine (Ismelin, discovered in the U.S.A. by Ciba Pharmaceutical Products).

D₂O boosts virus growth

Viruses multiply better in cells grown in heavy water (deuterium oxide) a scientist from the Wistar Institute, Philadelphia, told the New York Academy of Sciences recently.

Dr. D. Kritchevsky said that a weakened polio virus strain (known as the CHAT strain) which grows poorly on the standard (stabilised) culture of

monkey kidney cells in a normal water medium, grows well in the same cells when the medium contains water that is 40 to 50% deuterium oxide.

ISRAEL

Bromine production

Israel is third in the list of bromine producers, ranging immediately after the United States and Great Britain, according to the Dead Sea Bromine Works.

By bringing into operation an additional processing unit, this enterprise, situated in the Sodom area of the Negev, has increased output by about 50%. Israel's bromine exports are now shipped to 30 different countries, the latest being New Zealand. Only 4% of local production is consumed in Israel.

Chemical engineering firm

A new subsidiary of Haifa Fertilisers and Chemicals Ltd., Chemical Industry Equipment, supplies equipment to factories engaged in the production of chemicals, plastics and foodstuffs, and also to mining companies.

The subsidiary manufactures and designs pressure filters, special service pumps, mixers and reaction containers. It has also embarked on the design and supply of equipment for transportation of materials and, in co-operation with another enterprise, on the construction of cooling towers.

Present estimates indicate that a sum of I£100 million is to be invested in Israel's chemical industry, in the expansion of existing plants and in new enterprises. I£40 million (equal to about £8m. sterling) are earmarked for the purchase of equipment. Israel's local industry can manufacture not more than I£10 to I£12m. worth of the equipment required.

£26m. chemical industry

The turnover of Israel's chemical industry in 1959 totalled about I£130 million (approx. £26m. sterling). It comprises 350 larger and smaller plants with a total of 7,000 workers. The basic chemicals industry is on a very high level.

SOUTH AFRICA

Nicholas factory plan shelved

Plans made by Nicholas Products Ltd. to build a £250,000 garden factory at Pinetown, Natal, have been shelved for the time being. The company has decided to reconsider the project and introduce a new marketing strategy for its products. The factory would have covered 63,000 sq. ft. and the company had provided for extensions of 120,000 sq. ft. The plans took two years to complete. Building preliminaries started last December, after the Mayor of

Pinetown turned the first sod during a ceremony held on the site. The managing director of Nicholas Products said it had been decided to concentrate on the marketing of consumer goods that had a wide application to all sections of the community. Products with a limited specialist appeal would be discontinued. He said that international developments which had affected the Nicholas Group included the take-over by the parent company, Aspro-Nicholas Ltd., in Great Britain, of Griffiths Hughes Proprietaries Ltd., and the manufacturing and marketing arrangements made with Dow Chemical International Ltd., South Africa. "This agreement will broaden the scope and range of the company's veterinary division. Until these developments have been digested, the building of the new factory will have to be held over." To cope with urgent space requirements, alterations would be made to the existing factory in Congella Road, Durban.

Crocodile antidote

It seems that the tribal herbalists still have their secrets, for there is evidence to suggest that Africans in Central Africa have developed concoctions that effectively repel crocodiles. The usual method is to doctor the body with the secret preparation and then enter the water. When cattle have to be taken across a river infested with crocodiles they may be treated in the same way.

Drug plant opened

Wyeth Laboratories (Pty.) Ltd. have opened a £200,000 plant at Isando, near Johannesburg, for processing drugs and medicines. They intend to staff the entire plant with South Africans as they are trained.

BELGIUM

Du Pont to expand in Europe

A major portion of Du Pont's International manufacturing expansion is expected to take place in Europe, Lammot Du Pont Copeland, a vice-president and member of the Executive Committee of the company, declared at the opening of the new paint plant of Du Pont de Nemours (Belgium) S.A. recently.

BRITISH GUIANA

Drug imports

A new company, Pharmco (B.G.) Ltd., was recently registered with a share capital of 100,000 W. Indian dollars. Barclays Bank D.C.O. says the company will import and distribute to drug stores and doctors all types of drugs. It is associated with the Federal Pharmaceutical Co. Ltd. of Jamaica.

NEW TRADE MARKS

APPLICATIONS

Pharmaceuticals

BRIDAMOL.—796,201. *Calmic Ltd.*
 VANQUIN.—796,289. *Parke, Davis and Co.*
 PANAPED.—796,395. *British Drug Houses Ltd.*
 PFIZER.—756,108. *Chas. Pfizer and Co. Inc.*
 SPRAY-O-BAND.—B782,096. *Letchworth Pharmaceuticals Ltd.*
 CERUMOLEX.—785,481. *Jacob Rabinovitch.*
 ROX-ODIUM.—786,062. *Luscoe Products Ltd.*
 ZEPHISEGE.—790,963. *Bayer Products Ltd.*
 IWISE.—B791,561. *Austin Ibisson.*
 PROMIEL.—791,767. *Howard Lloyd and Co. Ltd.*
 SOBERETTE.—B794,236. *Sominex Ltd.*
 STAPHOSAN.—795,289. *Gascoigne-Crouther Ltd.*
 EXOTOL.—795,655. *Westminster Laboratories Ltd.*
 WINTLON.—796,575. *Bayer Products Ltd.*
 DALOMAX.—796,594. *Calmic Ltd.*
 GREOSIN.—790,957. *Glaxo Laboratories Ltd.*
 DIFARSINE.—792,244. *Union Chimique Belge S.A.*
 ESTERVAX.—793,080. *Willows Francis Ltd.*
 GELMATAB.—793,106. *Gale, Baiss and Co. Ltd.*
 ULCEAL.—793,129. *James Ballard.*
 MONOPULE.—793,511. *Bayer Products Ltd.*
 PANETS.—794,660. *Ward, Blinkinsop and Co. Ltd.*
 PROSAMORIN.—795,800. *May and Baker Ltd.*
 TERSAVID.—796,550. *Roche Products Ltd.*
 MOLUCID.—796,977. *I.C.I.*
 ORACON.—796,980. *I.C.I.*
 RESPULMON.—797,065. *Farbwerke Hoechst A.G.*
 GRAPINE.—785,182. *Gratine (Pty.) Ltd.*
 CLARIN.—B785,814. *Thos. Leeming and Co. Inc.*
 PRONEL.—789,540. *P. Leiner and Sons Ltd.*
 GERANICAT.—791,823. *A/B Bofors.*
 NICOPYRON.—791,959. *"Biosana" Dr. Med. Hans Krause.*

NEW PATENTS

COMPLETE SPECIFICATIONS ACCEPTED

Antibiotics

Process for fermentative production of antibiotics. *E. Belik, J. Doskocil, and M. Herold.* 831,125.
 Erythromycin esters of dicarboxylic acids. *Abbott Laboratories.* 830,846.
 1 - (2 - benzylaminoethyl) naphthalene and acid addition salts thereof, and pharmaceutical preparations of the penicillin salt. *Wellcome Foundation Ltd.* 830,913.

Detergents

Detergent compositions. *Shell Research Ltd.* 830,864.

Dyestuffs

Dyeing of fibrous materials or fibres. *G. W. Kunsch.* 830,348.
 Method for the continuous bleaching or dyeing of cellulosic fibres. *Smith and Nephew Textiles Ltd.* 829,835.
 Process for the preparation of oxidation dyestuffs on textile fibres. *Compagnie Française des Matières Colorantes.* 830,446.
 Finely crystalline pigment dyestuffs of the dioxazine series. *J. R. Geigy A.G.* 831,243.
 Water-soluble sulphonamide dyestuffs. *Imperial Chemical Industries Ltd., R. Price, C. H. Reece, and J. Wardleworth.* 830,246.
 Process for the production of oxidation dyeings or prints. *Farbenfabriken Bayer A.G.* 830,851.
 Printing and dyeing of pile fabrics. *Deep Dye Industries Inc.* 830,927.
 Process for dyeing polyamide or polyalkylene terephthalate fibres. *Howards of Ilford Ltd.* 831,141.
 Manufacture of monoazo-dyestuffs containing cobalt. *Farbwerke Hoechst.* 831,128.
 Dyes derived from iron complexes of α -nitroso- β -naphthols. *General Aniline and Film Corporation.* 829,917.
 Water-soluble azophthalocyanine dyestuffs. *Farbenfabriken Bayer A.G.* 830,920.
 Process for dyeing and impregnating animal leather. *Farbenfabriken Bayer A.G.* 830,841.

New patents are from the *Journal of Patents*, and new trade marks are from the *Trade Marks Journal*. In each case permission to publish has been given by the controller of Her Majesty's Stationery Office. Each of the publications mentioned is obtainable from the Patent Office, 26 Southampton Buildings, London, W.C.2.

Symmetrical indigoid dyestuffs and process for their manufacture. *Ciba Ltd.* 831,810

Fertilisers

Process of preparing a compound fertiliser containing nitrate of ammonia and dicalcium phosphate, from sedimentary phosphates. *Stamcarbon N.V.* 830,815.

Pesticides

Agricultural chemical compositions. *Fisons Pest Control Ltd.* 831,344.
 Fungicidal products. *Murphy Chemical Co. Ltd., and M. Pianka.* 830,650.
 Fungicidal compositions. *Pittsburgh Coke and Chemical Co.* 829,879.
 Pest-combating preparations. *Ciba Ltd.* 831,075.
 Thiocyanic esters and pesticidal compositions containing them. *Soc. des Usines Chimiques Rhône-Poulenc.* 831,420.
 Pesticidal compositions. *Lunvale Products Ltd., and M. Fitzgibbon.* 831,790.

NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C.2.

Joly and Bradburn Ltd. 22.2.60. 224A Havant Rd., Drayton, Portsmouth. Chemists and druggists. £7,500. Dirs.: G. Joly, A. B. Bradburn.

C. M. Watson Ltd. 22.2.60. 239 Roundhay Rd., Leeds 8. Chemists, etc. £6,000. Dirs.: Cecil M. O. and Mrs. N. Watson.

W. Raynor (Chemist) Ltd. 24.2.60. 10 Park Square, Leeds 1. £1,000. Dir.: Wilfred Raynor.

George King (Pharmaceuticals) Ltd. 25.2.60. 43 Upper Berkeley St., London, W.1. £100. Dirs.: Harry Judd, F. A. Webber and R. G. Cook.

Farley and Co. (London) Ltd. 11.2.60. 56 Avenue Chambers, Vernon Place, London, W.C.1. Chemists. £100. Dir.: Eric S. Farley.

R. Harold Cash Ltd. 11.2.60. 7 Whetstone Hey, Great Sutton, Wirral, Cheshire. Chemists, druggists and opticians. £1,000. Dirs.: R. H. and Margaret Cash, and Eric T. Rogers.

Wilsons Pharmacy Ltd. 11.2.60. 34 Windsor Rd., Thornley Park, Denton, Lancs. £2,000. Dirs.: June P. and May Wilson.

Hamilton Blears Ltd. 12.2.60. 215 Brinkway, Stockport. Mfrs. of and dls. in chemicals, drugs, etc. £100. Dirs.: Mrs. G. M. and Leonard G. Blears, and T. J. Owen.

Sixty-Five Years Ago

From MANUFACTURING CHEMIST
 July 1895

Microbes in Railway Carriages

One of those ingenious scientists who make it their duty to apprise us of the fearful risks we every day incur and supply us with figures to prove it—figures which no one takes the trouble to prove or disprove—has just ascertained that on the Russian portion of the line between St. Petersburg and Berlin, 16,000 microbes to the cubic inch travel first class, 34,000 second and 78,000 third class. Thus it will be seen that travellers have at least something wherewith to while away the tedium of a long journey.

Manufacturing Chemist's ENQUIRY BUREAU

Leonard Hill House, Eden Street, London, N.W.1.

Subscribers requiring names of suppliers of chemicals or plant should state their needs on this form, giving approximate quantities, clip it to their business noteheading and send it to the Bureau, as above. Please type or use block letters.

For office use

No.

Date.

